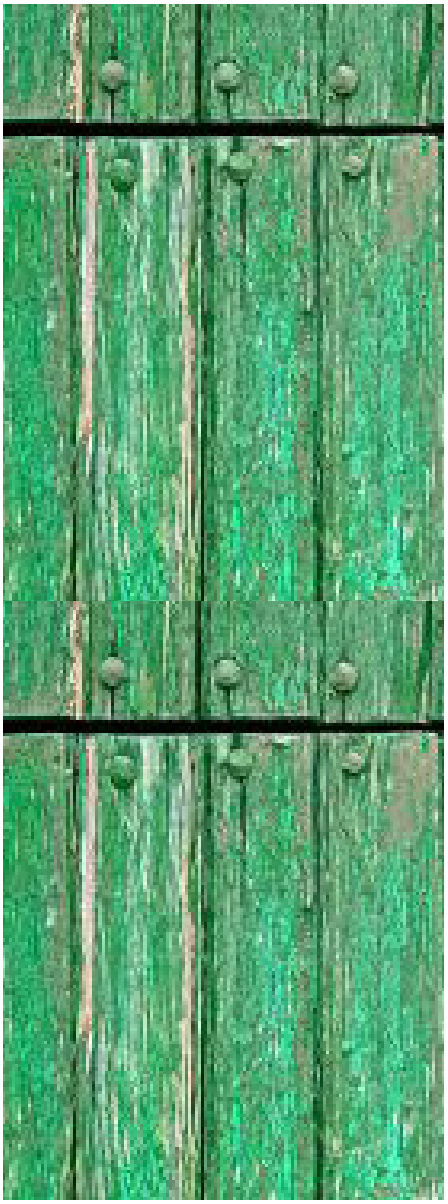
BROUGHT BACK DUE TO POPULAR DEMAND

The Editor and Writer of this Opinion Piece is a Pastor and an Earnest Commentator on Matters of Revivalism and Church Profile Globally

The PROPHETIC CALLING OF THE MAN OF GOD

Getting to know the concealed side of the Prophet

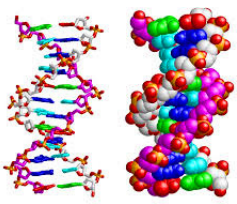
By EDITOR & STAFF WRITER



University of Haifa, on Mount Carmel, Haifa, Israel

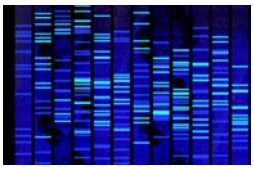
ON MOUNT CARMEL-ISRAEL

The MAN OF GOD THE PROPHET is a *Scholar* who in His days prior to the *calling* of the LORD, had deeply *entrenched* Himself into serious *cutting-edge* Cancer Research in the United States of America. This is what took Him across different medical schools, at which He left His unmistakable stripes in *Academia*. However, when He enrolled for His



first degree at Makerere University and took up His residence at the Northcourt Hall, little did the MAN OF GOD know that GOD ALMIGHTY had as a matter of fact a totally different plan for His life. Barely had He began His first year Bachelor of Science Program at Makerere, than He was compelled to transfer back to the University of Nairobi owing to the brutal civil war that broke out in Uganda between Museveni's NRA and the establishment. Upon completing His first and masters degree programs at the University of Nairobi, the world appeared to have opened up many life career opportunities right in front of Him. However, it was while in His masters degree program, that behind the scenes, GOD ALMIGHTY was already beginning to *engineer* the course of His life in a totally different direction.

PCR Thermocycler The kind that the MAN OF GOD used for DNA Sequence Analysis



This *divine* intervention by the LORD began to clearly take shape in the most unusual way, when He finally struck all straight A's in His masters degree academic course work, at the University of Nairobi. This is what caused Him to attract several scholarships from abroad and most *notably* from Israel. In that way, the LORD deliberately

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Phosphorylation of Transcriptional Coactivator Peroxisome Proliferator-activated Receptor (PPAR)-binding Protein (PBP)

STIMULATION OF TRANSCRIPTIONAL REGULATION BY MITOGEN-ACTIVATED PROTEIN KINASE*

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Parimal Misra‡§, Edward D. Owuor¶, Wenge Li¶, Songtao Yu‡, Chao Qi‡, Kirstin Meyer‡, Yi-Jun Zhu‡, M. Sambasiva Rao‡, A.-N. Tony Kong¶, and Janardan K. Reddy‡‖

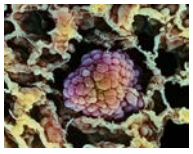
From the ‡Department of Pathology, The Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611–3008, the ¶Department of Pharmaceutics, College of Pharmacy, Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, New Jersey 08854–8020, and §Discovery Research, Dr. Reddy's Laboratories Ltd., Miyapur, Hyderabad 500050, India

Peroxisome proliferator-activated receptor (PPAR)-binding protein (PBP) is an important coactivator for PPARγ and other transcription factors. PBP is an integral component of a multiprotein thyroid hormone receptor-associated protein (TRAP)/vitamin D_3 receptor-interacting protein (DRIP)/activator-recruited cofactor (ARC) complex required for transcriptional activity. To study the regulation of PBP by cellular signaling pathways, we identified the phosphorylation sites of PBP. Using a combination of *in vitro* and *in vivo* approaches and mutagenesis of PBP phosphorylation sites, we identified six phosphorylation sites on PBP: one exclusive protein kinase A (PKA) phosphorylation site at serine 656, two protein kinase C (PKC) sites at serine 796 and serine 1345, a common PKA/PKC site at serine 756, and two extracellular signal-regulated kinase 2 sites of the mitogen-activated protein kinase (MAPK) family at

superfamily participate in diverse biological processes such as early development, cell proliferation, differentiation, apoptosis, metabolic homeostasis, and cancer (1–4). Liganded nuclear receptors engage in these pivotal processes by controlling gene expression patterns in a cell- and gene-specific manner by interacting with specific DNA sequences in the promoter regions of target genes and by recruiting a plethora of transcriptional coactivators (3, 5–7). Coactivators that have been cloned in recent years include the p160/steroid receptor coactivator-1 (SRC-1) family with three members (SRC-1, TIF2/GRIP1/SRC2, and pCIP/ACTR/AIB1/RAC3/TRAM1/SRC-3) (8–14), cAMP-response element-binding protein-binding protein (CBP) (15), adenovirus E1A-binding protein p300 (16), PPAR-binding protein PBP (TRAP220/DRIP205) (17, 18), and many others (5, 7, 19–25). It is becoming increasingly evident that these coactivators enhance the transcriptional activity not only of nuclear

orchestrated a *major* move when all of a sudden, a Professor who was an American Jew from Israel *appeared* and demanded to meet the MAN OF GOD. When that meeting realized at the Fairview Hotel in Nairobi, the Professor informed Him that the University had advanced the MAN OF GOD'S name to him as a top student for scholarship. With the German Academic Exchange Program (DAAD scholarship) already awarded to Him, it was the most unusual thing for the MAN OF GOD to have rejected that lucrative German scholarship, in favour of the less paying Israeli sponsorship. Only the move of GOD could explain such an *irrational* decision at a time when all that mattered was student *stipend*. That is what *propelled* the PROPHET OF THE LORD towards gaining contact with Israel, in an encounter that would later turn out to be the shaper of His *destiny with GOD*. After attending Ben Gurion University of the Negev in Israel for His Masters thesis on the biochemistry of *Iso-enzymes*, owing to His excellent performance, the MAN OF GOD THE PROPHET was rapidly admitted into a Ph.D Program at the University of Haifa on MT. CARMEL. At that time, nothing seemed to cross His mind that all this positioning on MT. CARMEL was as matter of fact, the deliberate doing of the LORD. At the University of Haifa, the MAN OF GOD majored His Ph.D Thesis work on *DNA multilocus structures* and sequence comparisons for molecular expressions. He conducted an *indepth* study on DNA Polymorphism in which

The Cancer Research Lab



Lung Tumour

Analysing Cancer Cells

Institute for Genetics, Universitat Gießen

He examined the Random Amplified Polymorphic DNA (RAPDs) using several synthetic *oligonucleotides*. This caused Him to *major* in the DNA Polymerase Chain Reaction (PCR) Techniques as a novel means of studying sequence comparison and polymorphism analysis. Moreover, His doctoral thesis also took Him to the Institute For Genetics of the University of Giessen in Germany, where he further studied DNA sequences that code for resistance to viral infections. While on MT. CARMEL, the MAN OF GOD

BEN GURION UNIVERSITY OF THE NEGEV

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Activation of Mitogen-activated Protein Kinase Pathways Induces Antioxidant Response Element-mediated Gene Expression via a Nrf2-dependent Mechanism*

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Rong Yu‡§, Chi Chen‡§, Yin-Yuan Mo‡, Vidya Hebbar‡§, Edward D. Owuor‡§, Tse-Hua Tan¶, and A.-N. Tony Kong‡§‖

From the ‡Department of Pharmaceutics and Pharmacodynamics and §Center for Pharmaceutical Biotechnology, College of Pharmacy, University of Illinois, Chicago, Illinois 60612 and the ¶Department of Immunology, Baylor College of Medicine, Houston, Texas 77030

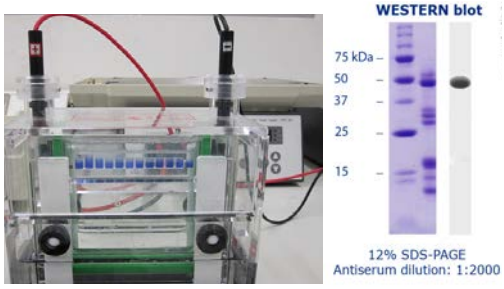
Antioxidant response element (ARE) regulates the induction of a number of cellular antioxidant and detoxifying enzymes. However, the signaling pathways that lead to ARE activation remain unknown. Here, we report that the expression of mitogen-activated protein (MAP) kinase/extracellular signal-regulated kinase kinase kinase 1 (MEKK1), transforming growth factor-β-activated kinase (TAK1), and apoptosis signal-regulating kinase (ASK1) in HepG2 cells activated the ARE reporter gene, whereas the expression of their dominant-negative mutants impaired ARE activation by the chemicals sodium arsenite and mercury chloride. Coexpression of downstream kinases, MAP kinase kinase 4, MAP kinase kinase 6, and c-Jun NH_2-terminal kinase-1, but not MAP kinase kinase 3 and p38, augmented ARE activation by MEKK1, TAK1, and ASK1. The coexpression of a basic leucine zipper transcription factor Nrf2 but not c-Jun also greatly enhanced the activation of reporter gene by MEKK1, TAK1, and ASK1; however, a dominant-negative mutant of Nrf2 (NF-E2-related factor 2) blocked this event. Furthermore, when overexpressed, MEKK1, TAK1, and ASK1 induced the expres-

coupling various extracellular signals to a variety of biological processes, such as gene expression, cell proliferation, differentiation, and cell death (1, 2). To date, at least six MAPK members have been identified in mammalian cells. Three of the MAPK members have been extensively studied: extracellular signal-regulated kinases (ERK) (3), c-Jun NH_2-terminal kinases (JNKs, also called stress-activated protein kinases) (4, 5), and p38 (6, 7). The activity of these MAPKs is induced through the phosphorylation of their threonyl and tyrosyl residues within a tripeptide motif TXY by a dual specificity kinase termed MAP kinase kinase (MKK), which in turn is phosphorylated and activated by an upstream kinase generally called MAPK kinase kinase (MAPKKK) (8). The first MAPKKK identified is Raf-1. This kinase activates ERK through MEK1 or MEK2 but has little effect on JNK and p38 pathways (1). However, unlike Raf-1 MEKK1, a MAPKKK isolated after Raf-1 predominantly stimulates JNK activity that is mediated by MKK4 or MKK7 (9). Recently, several other members of the MAPKKK family have been identified including TAK1 (10) and ASK1 (11). These kinases are able to activate JNK through MKK4 and p38 through MKK3 or MKK6, but they do not affect

THE PROPHET received a *National Award* as the top doctoral student of the program in that year.

DESIGNING
Anti-cancer Drugs

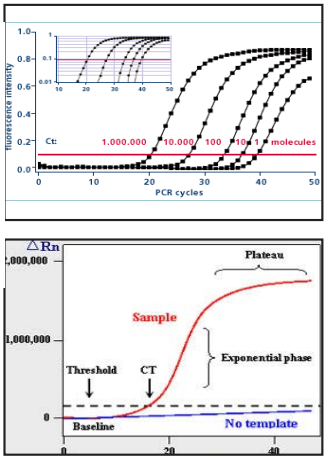
Upon the completion of His Doctorate from the University of Haifa on MT CARMEL in Israel, the MAN OF GOD THE PROPHET was immediately offered appointment in two leading institutions of Medicine in the US. The first being the Centre for Advanced Biotechnology and Medicine (CABM) of the University of Medicine & Dentistry of New Jersey (UMDNJ); and the other being the Centre for Pharmaceutical Biotechnology of the University of Illinois at Chicago (UIC). The MAN OF GOD THE PROPHET then decided to take up the appointment at the Centre for Pharmaceutical Biotechnology of the University of Illinois at Chicago. He took up the esteemed position of *Post-Doctoral Associate* at the Prestigious Centre of Excellence,



Western Blot System that the MAN OF GOD used for analysing expression of MAPK Oncogenes through the SDS-Polyacrylamide gels and antibody detection of gene amplification.

the Center for Pharmaceutical Biotechnology in Chicago. The MAN OF GOD then got deeply involved in research and teaching within the Department of *Pharmacokinetics* and *Pharmacodynamics* of the UIC College of Pharmacy. In that position, the MAN OF GOD worked in the area of *Drug Metabolism* and specifically specialized in *Signal Transduction by Cancer Chemotherapeutic Drugs*. This is a specialized branch of medicine that examines the different biochemical pathways elicited in the human body by different medications. This included the respective *cellular cytotoxicity* pathways and side effects that lead to *hair loss, liver failure* and subsequent *death* among cancer patients. It is then that He developed particular interest and majored in the novel field of *signal transduction by cancer chemotherapeutic drugs* for the different types of *carcinomas*.
He also *instructed* Doctor of Pharmacy (PharmD), undergraduate, and Ph.D students, whose programs were affiliated with the Centre for

The kind of Q-PCR machine that the MAN OF GOD used to run Real Time PCR Amplification Analysis of Cancer Genes



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Epigallocatechin-3-gallate-induced stress signals in HT-29 human colon adenocarcinoma cells

Chi Chen, Guoxiang Shen, Vidya Hebbar, Rong Hu, Edward D.Owuor and A.-N.Tony Kong[1]

Department of Pharmaceutics, Ernest-Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

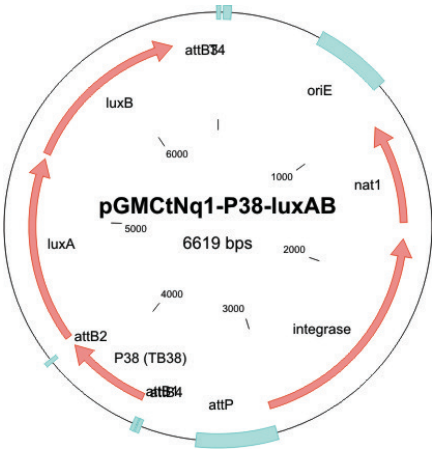
[1]To whom correspondence should be addressed
Email: kongt@cop.rutgers.edu

Epigallocatechin-3-gallate (EGCG), a major component in green tea polyphenols, has been proven to suppress colonic tumorigenesis in animal models and epidemiological studies. As EGCG is retained in the gastrointestinal tract after oral administration, this pharmacokinetics property gives it the potential to function as a chemopreventive agent against colon cancer. In this study, human colorectal carcinoma HT-29 cells were treated with EGCG to examine the anti-proliferative and pro-apoptotic effects of EGCG, as well as the molecular mechanism underlying these effects. Cell viability assay, nuclear staining, DNA fragmentation, caspase assay, cytochrome *c* release, $DiOC_6(3)$ staining, mitogen-activated protein kinases (MAPK) phosphorylation and trypan blue exclusion assays, were utilized to dissect the signaling pathways

Korea, one of the prominent lifestyles is the daily consumption of green tea drinks by a large population. Chemically, the water-extractable fraction of green tea contains abundant polyphenolic compounds, in which epigallocatechin-3-gallate (EGCG) is the major constituent (>50% of polyphenolic fraction). After a common brewing procedure, 30–42% (w/w) of green tea can be dissolved in water. Therefore, a single cup of green tea can contain up to 200 mg of EGCG (3). The cancer prevention effect of green tea and EGCG against various tumors has been proven with numerous animal models (4,5). Human clinical trials, although inconclusive, also indicated some positive link between the drinking of green tea and the decrease of cancer incidence (6). In rodent models for determining the pharmacokinetics profile of green tea catechins, the highest tissue concentrations of EGCG have always been found in the intestine after either oral or i.v. administrations (7–9). Furthermore, substantial amounts of EGCG were present in human colon mucosa samples from the patients drinking tea 12 h before colorectal surgery (4). Because of this pharmacokinetic profile, as well as the high local concentration in intestinal microenvironment that come from direct contact of green tea drinks with colon mucosa, the

Pharmaceutical Biotechnology. The MAN OF GOD THE PROPHET at that time, conducted ground-breaking *research* on several types of cancers, including cervical carcinoma and HT-29 human colon cancer. It was during that time that the PROPHET OF THE LORD went deep into studying *oncologically* important proteins known as *onco-protein* networks. These are the networks of proteins that modulate *cancer growth* and *development* in the human body. It is an expedition that caused the MAN OF GOD to deeply explore members of the *serine/threonine* protein super family. These group of important proteins are the by-products of onco-gene expression, and encompass a larger network of *polypeptides* that are critical in *cancer growth* and *development*. It is this crucial role that such peptides play in oncogenesis that endears them as potential future drug targets for novel cancer therapy. Among the *serine/threonine* super family, the MAN OF GOD THE PROPHET particularly gained deeper interest in studying the subgroup known as the *Mitogen Activated Protein Kinases* (MAPKs). This is what propelled the MAN OF GOD to do an extensive research on *signalling* by cancer chemotherapeutic drugs, and how such compounds can be used to *target* and *disrupt* some of these biochemical *pathways* that cancers so vastly *exploit* for their growth. It was while examining the *mitogen-activated onco-protein* networks that the MAN OF GOD extensively studied the different human carcinomas and how they showed differential signalling pathways for *growth, proliferation* and *drug resistance*. This is what pushed Him right into the novel field of *receptor science*, at which He examined *receptor trimerization* and *receptor-protein* recruitment complexes that are often drug targets on *cell membranes*. The cancers whose signalling pathways the MAN OF GOD examined in greater detail included cervical carcinoma, breast cancer, lung cancer, and HT-29 model of human colon carcinomas. In that indepth research undertaking, it was while examining the MAPK *onco-protein* networks that the MAN OF GOD

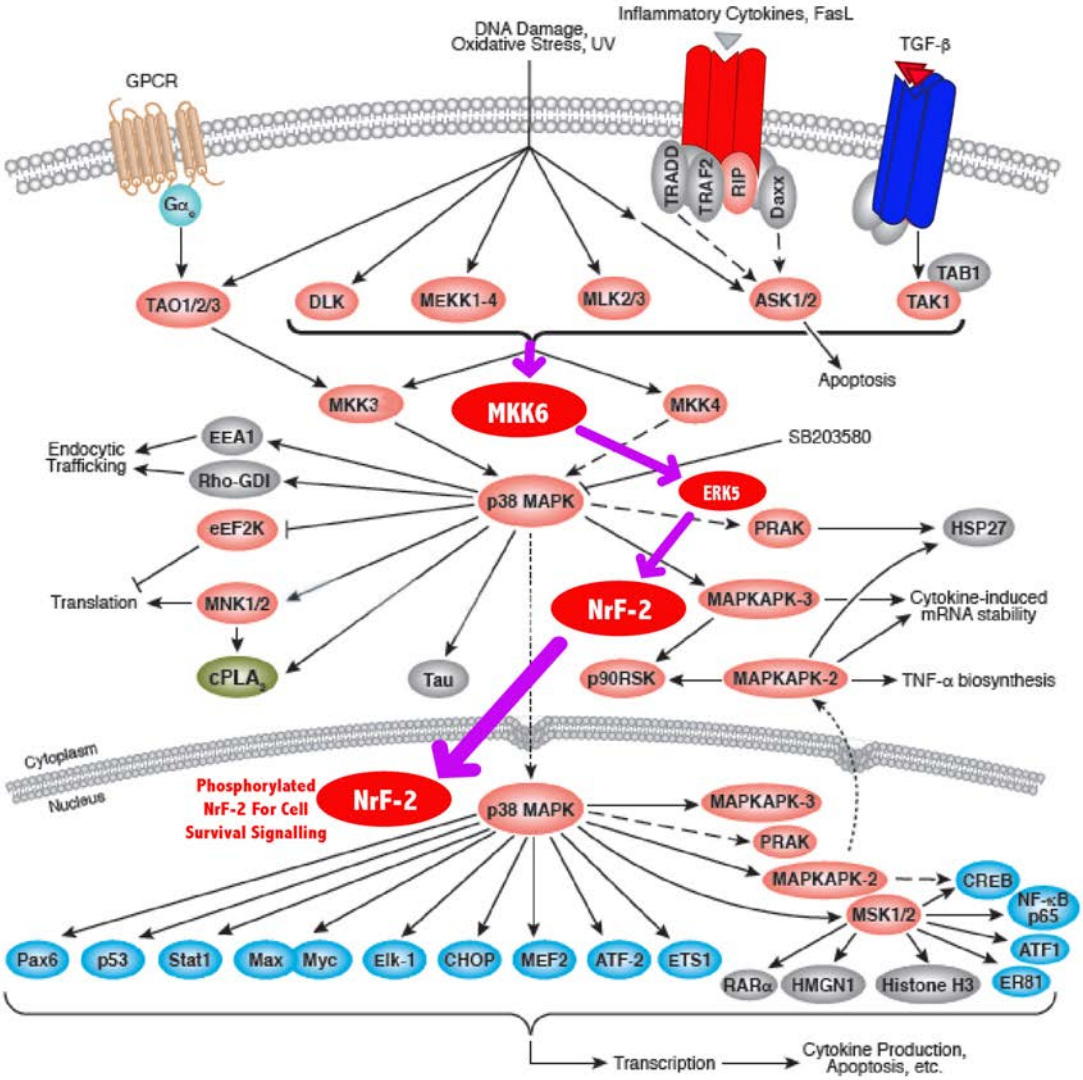
Ernest Mario School of Pharmacy



p38 plasmid construct that the MAN OF GOD used for invitro studies of oncogenes for gene expression & transgenic studies

The Cross-talk between ERK5 Signaling & p38 MAP Kinase Pathways that the Man Of God discovered which compromises Anti-Cancer Drug Therapy

(The MAN OF GOD published this discovery in the JOURNAL OF BIOCHEMICAL PHARMACOLOGY -Vol 64, Issues 5-6, September 2002, Pages 765-770)



became the first person to discover that the cell *self-suicide p38 pathway*, known as *apoptotic signalling*, as a matter of fact CROSS-TALKED with cell *proliferation* and *survival* pathways such as the Extra-cellular Regulated Kinases 1 & 2 (ERK1/2). Moreover, when a new Extra-cellular Regulated Kinase oncogene 5 (ERK5) was cloned from the mouse, the MAN OF GOD was the first to give it an extensive cancer signalling study. The PROPHET OF THE LORD was driven by the urge to know how this new ERK5 activated and fired signals in relation to the traditionally known ERK1/2. To do this, He challenged it in co-transfection gene transfer studies with *p38* construct of MAPKs (*see construct above*). It is through this extensive study that the MAN OF GOD then discovered that the CROSS-TALK that He discovered between the said *onco-genes* actually occurs via the intermediary *onco-gene* protein called MKK6. This became a novel finding, thereby making the MAN OF GOD the first person to discover that this is what seriously compromises *cancer drug therapy*, and leading to drug resistance among cancer patients. It is the main cause of eventual deaths of cancer patients despite being on recommended *chemotherapeutic* regimen. The MAN OF GOD also got interested in studying the growth and development of human *hepatoma*.

ANTI-CANCER PROPERTIES OF QUINACRINE & DERIVATIVE DRUGS

While examining the human *cervical carcinoma*, the MAN OF GOD also became interested in studying how *Quinacrine*, a *Phospholipase-A2* inhibitor exerted its cancer *chemotherapeutic* properties. Whereas *Quinacrine* had been extensively used in the clinical treatment of various anti-cancer related conditions, such as intra-cavitary treatment of malignancies, its signaling pathways however had not been mapped out biochemically. It was during that time that the MAN OF GOD made some significant ground-breaking discoveries regarding the

Arch Pharm Res Vol 24, No 2, 126-135, 2001 Pharmacology, Toxicology & Pharmaceutic

Quinacrine Induces Cytochrome c-dependent Apoptotic Signaling in Human Cervical Carcinoma Cells

Adedigbo A. Fasanmade[1,2], Edward D. Owuor[1, 3], Rachel P. L. Ee[1], Dima Qato[1], Mark Heller[2], and Ah-Ng Tony Kong[1,3]

[1]Department of Pharmaceutics and Pharmacodynamics, Center for Pharmaceutical Biotechnology, College of Pharmacy, [2]Present address: Centocor Biotechnologies Inc., 200 Great Valley Parkway, Malvern, PA 19355, USA, [3]Department of Pharmaceutics, College of Pharmacy, Rutgers University, Environmental and Occupational Health Sciences Institute, 170 Frelinghuysen Road, Piscataway, NJ 08854, USA [4]Deparment of Hematology/Oncology, College of Medicine, University of Illinois at Chicago, Chicago, IL 60607, USA
1st and 2nd authors contributed equally to this paper

(Received December 23, 2000)

Quinacrine (QU), a phospholipase-A2 (PLA-2) inhibitor has been used clinically as a chemotherapeutic adjuvant. To understand the mechanisms leading to its chemotherapeutic effect, we have investigated QU-induced apoptotic signaling pathways in human cervical squamous carcinoma HeLa cells. In this study, we found that QU induced cytochrome c-dependent apoptotic signaling. The release of pro-apoptotic cytochrome c was QU concentration- and time-dependent, and preceded activation of caspase-9 and -3. Flow cytometric FACScan analysis using fluorescence intensities of $DiOC_6$ demonstrated that QU-induced cytochrome c release was independent of mitochondrial permeability transition (MPT), since the concentrations of QU that induced cytochrome c release did not alter mitochondrial membrane potential ($\blacktriangle \Psi_m$). Moreover, kinetic analysis of caspase activities showed that cytochrome c release led to the activation of caspase-9 and downstream death effector, caspase-3. Caspase-3 inhibitor (Ac-DEVD-CHO) partially blocked QU-induced apoptosis, suggesting the importance of caspase-3 in this apoptotic signaling mechanism. Supplementation with arachidonic acid (AA) sustained caspase-3 activation induced by QU. Using inhibitors against cellular arachidonate metabolism of lipooxygenase (Nordihydroxyguaiaretic Acid, NDGA) and cyclooxygenase (5,8,11,14-Eicosatetraynoic Acid, ETYA) demonstrated that QU-induced apoptotic signaling may be dependent on its role as a PLA-2 inhibitor. Interestingly, NDGA attenuated QU-induced cytochrome c release, caspase activity as well as apoptotic cell death. The blockade of cytochrome c release by NDGA was much more effective than that attained with cyclosporin A (CsA), a MPT inhibitor. ETYA was not effective in blocking cytochrome c release, except under very high concentrations. Caspase inhibitor z-VAD blocked the release of cytochrome c suggesting that this signaling event is caspase dependent, and caspase-8 activation may be upstream of the mitochondrial events. In summary, we report that QU induced cytochrome c-dependent apoptotic signaling cascade, which may be dependent on its role as a PLA-2 inhibitor. This apoptotic mechanism induced by QU may contribute to its known chemotherapeutic effects.

Key words: Quinacrine, Cytochrome c, Caspase-3; Phospholipase-A-2; Cervical Carcinoma, Apoptosis

potential of Quinacrine being used as a cancer chemotherapeutic drug that can address specific therapeutic targets in cervical carcinoma. He hence became the first person to discover that *Quinacrine,* which is often clinically referred to as *mepacrine*, was yet another chemical agent that offered a very great potential in cancer therapy. While in its traditional pharmaceutical value *Quinacrine* had been used for a long time as an anti-malarial drug, its use as an antibiotic cannot be underated. Furthermore, its cancer *chemotherapeutic* potential had also been widely explored for the clinical management of different malignancies. Therefore, *Quinacrine* which is also popularly abbreviated to as *QU* in pharmaceutical circles, has also been extensively used to treat *giardiasis*, a *protozoal* infection of the intestinal tract, and certain types of *lupus erythematosus*, an inflammatory disease that affects the joints, tendons, and other connective tissues and organs. In such applications nonetheless, *Quinacrine* was routinely injected into the space surrounding the lungs to prevent reoccurrence of *pneumothorax*. While it may have been suspected that *Quinacrine* might be exerting its pharmaceutical properties through its ability to inhibit *interferon induced trafficking* of *neutrophils*, the *biochemical signalling pathways* that it activates remained virtually unknown. NONETHELESS, when the MAN OF GOD THE PROPHET decided to investigate *Quinacrine* as a *model drug* for *cancer chemotherapy*, it was incredible that after investing three years into that research project, He finally made a breakthrough when He became the first person to discover that *Quinacrine* as a matter of fact, had its own *cancer chemotherapeutic properties*, that enabled it to kill human cervical cancer. This discovery delianated *Quinacrine* from its role as a *chemotherapeutic adjuvant*, and established it as a cancer *chemotherapeutic agent* that exploits *cytochrome-c pathway* on its own merit. After that discovery, it then became necessary for the MAN OF GOD to confirm His theory by employing *invitro* studies of cancer cells in order to *elucidate* the *biochemical signalling pathways* that *Quinacrine* employs to exert its potent *chemotherapeutic properties*. It is this potency that permitted *Quinacrine* and related class of drugs to kill cancer cells in the human body. That is when the MAN OF GOD made serious *in-roads* in dissecting the *signal transduction biochemical pathways* that *Quinacrine* exploits in order to distrupt the growth of cervical cancer. This is the ground-

Environmental & Occupational Health Sciences Institute: Where the MAN OF GOD'S office was located.

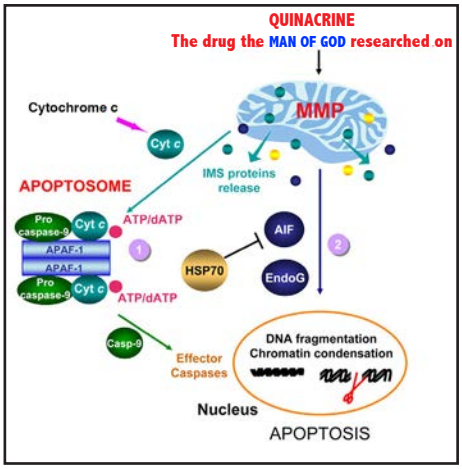
breaking research that led the MAN OF GOD to discover that *Quinacrine* indeed exerted its cancer *chemotherapeutic* properties through the *mitochondrial cytochrome-c* dependent *pathway*. It became a major *finding* because such a class of drugs can then be used to target the *ATP synthesis pathways* by *disrupting* the *Mitochondrial Membrane Pore Transition Permeability Potential* (MPT/PTP). The MAN OF GOD then fully embarked on a major rigorous *biochemical expedition* by using *western blots* and the flamboyant *Flow Cytometry* technology with iodide staining of cancer cells, to thoroughly investigate how the cancer *mitochondrial membrane* integrity can be *targeted* by chemotherapeutic drugs. That is when the MAN OF GOD discovered and scientifically verified using the DIOC6 staining dye that *Mitochondrial membrane* potential of cervival cancer cells are effectively *targeted* and *disrupted* by cancer chemotherapeutic drugs, and especially *Quinacrine*. *Quinacrine* had now become '*the new kid on the block*' that the MAN OF GOD had just discovered. That study became a serious benchmark for drug discovery and design because it yielded significant clues on how *cytochrome-c* release could now become a very important mechanism of *detection* of the *effectiveness* of cancer therapeutic agents that *target* and *disrupt* the *mitochondria* of the cancer cells.

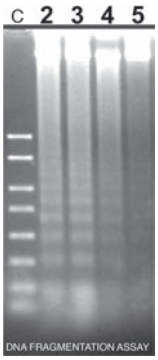
Flow Cytometry machine that the MAN OF GOD used to analyse cytochrome-c release in cancer.

Moreover, it became a study that opened up a new paradigm on how *cytochrome-c* couples with *Pro-Caspase-9* to form *cytochrome c-Pro Caspase-9 protein complex*. It is this *cytochrome-c Pro-Caspase-9 complex* that bore the capacity to activate and release active *Caspase-9* which then fired up the signal to activate the cell death downstream *Caspace-3* which then leads to *DNA Cleavage and fragmentation* in a process known as *Apoptosis* of cancer cells. That is when the MAN OF GOD got directly involved with a team of Professors who were deeply engaged in front-line drug design and drug discovery for cancer *chemotherapy*.

MOLECULAR MEDICINE

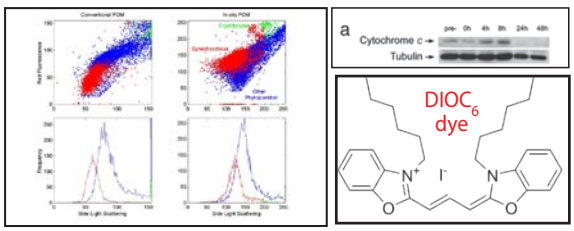
The novelty of His work arose from the fact that *molecular medicine* of the kind He was pursuing, has superiority over the present-day conventional medicine, because that system of molecular signaling would result into new kinds of *future therapies*. This kinds of future drugs from *molecular medicine* will encompass small DNA *oligonucleotide molecules*, and small *protein peptides*, which can be administered to cancer patients to avert the massive *side effects* they suffer. The kind of medications the MAN OF GOD was working on are those that would exploit *gene transfer* and *transgenics* which don't impose significant side effects on cancer patients. The *side effects* of cancer chemotherapy that the MAN OF GOD THE PROPHET was working against, are those catalogued by the American Society for Clinical Oncology, and they included the following side effects that cancer patients tremendously suffer: tiredness (fatigue), nausea, and vomiting, diarrhoea and abdominal cramping, low white blood cell count, mouth sores (Mucositis), Myelosuppression which means the bone marrow stops producing blood cells, and also nerve damage known as *peripheral neuropathy*, which leads to tingling, numbness and pain in the hands and feet. Occasionally, these side





THE DNA Fragmentation ASSAY that shows the proof of DNA Cleavage by the Cancer Chemotherapeutic Agent, in this case QUINACRINE

effects become very *life-threatening* if not well managed, and that is why the MAN OF GOD focussed on molecular medicine of discovering new molecular *DNA* and *peptide* drugs that would evade these *side effects*. Arising from His cancer works published extensively at that Centre for Pharmaceutical Biotechnology, He extensively published and co-authored His findings with top-notch Professors involved in cancer research, treatment, management and care, in world class peer review Cancer Research Journals. These included the most coveted *Journal for Biological Chemistry* (JBC; www.jbc.org), *Journal For Pharmaceutical Research*, *Journal of Carcinogenesis*, *Mutation Research Journal*, and *Drug Metabolism Review Journal*. The PROPHET OF THE LORD also



Flow Cytometry Computer Cluster Analysis of $DIOC_6$ Staining of Mitochondria to gauge Membrane damage and change of Membrane Permeability Transition Potential (MPT) and the consequent cytochrome-c release that the MAN OF GOD performed on Cancer Cells.

Journals

Biochemical Pharmacology
Volume 64, Issues 5–6, September 2002, Pages 765–770
Cell Signaling, Transcription and Translation as Therapeutic Targets

Antioxidants and oxidants regulated signal transduction pathways ☆

Edward D. Owuor, Ah-Ng Tony Kong
Department of Pharmaceutics, Ernest Mario School of Pharmacy, and the Environmental and Occupational Health Sciences Institute (EOHSI), Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

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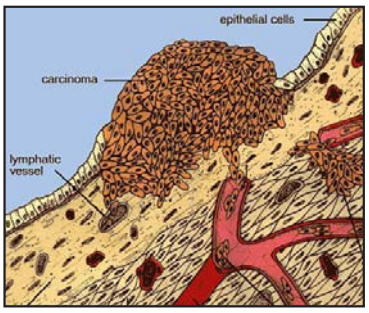
Abstract

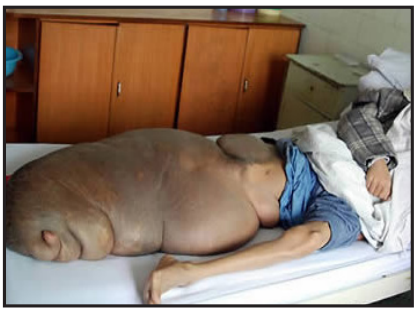
Many drugs and xenobiotics induce signal transduction events leading to gene expression of either pharmacologically beneficial effects, or unwanted side effects such as cytotoxicity which can compromise drug therapy. Using dietary chemopreventive compounds (isothiocyanates and green tea polyphenols), which are effective against various chemically-induced carcinogenesis models in animals studies, we studied the signal transduction events and gene expression profiles. These compounds have typically generated cellular "oxidative stress" and modulated gene expression including phase II detoxifying enzymes GST and QR as well as cellular defensive enzymes, heme oxygenase 1 (HO-1) and *GSTvia* the antioxidant/electrophile response element (ARE/EpRE). Members of the bZIP transcription factor, Nrf2 which heterodimerizes with Maf G/K, were found to bind to ARE, and transcriptionally activate ARE. Additionally the mitogen-activated protein kinases (MAPK; ERK, JNK and p38) were differentially activated by these compounds, and involved in the transcriptional activation of ARE-mediated reporter gene. Transfection studies with various cDNA encoding for wild-type of MAPK and Nrf2 showed synergistic response during co-transfection and to these agents. However, by increasing the concentrations of these xenobiotics, caspase activities and apoptosis were observed which were preceded by mitochondria damage and cytochrome *c* mitochondria release. Further, increased concentrations led to rapid cell necrosis. DNA microarray analyses were performed to ascertain the gene expression profiles elicited by these compounds at low concentrations as well as at higher concentrations. Thus, we have proposed a model, that at low concentrations, these compounds activate MAPK pathway leading to activation of Nrf2 and ARE with subsequent induction of phase II and other defensive genes which protect cells against toxic insults thereby enhancing cell survival, a beneficial homeostatic response. At higher concentrations, these agents activate the caspase pathways, leading to apoptosis, a potential cytotoxic effect if it occurred in normal cells. The studies of these signaling pathways may yield important insights into the pharmacodynamic and toxicodynamic effects of drugs and xenobiotics during pharmaceutical drug discovery and development.

Abbreviations

published a complete *authoritative* review paper that gave a broader overview in the discipline of *signal transduction* by oxidants like *Reactive Oxygen Species* (ROS) and their role in the processes of malignancy like *carcinogenesis*, *tumorigenesis* and *oncogenesis*. In that extensive review published in the *Journal for Biochemical Pharmacology*, the MAN OF GOD also looked at the role of anti-oxidants in *cancer chemoprevention*.



The kind of deadly carcinoma that the MAN OF GOD worked on.



Advanced stage cancer on the right leg

(National Library of Medicine-Pubmed; NCBI).

UNVEILING GENE SWITCHES IN CANCER CHEMOTHERAPY

In His *colourful* career tenure track, the MAN OF GOD was further appointed to the Department of Pharmaceutics at the Ernest Mario School of Pharmacy at the State University of New Jersey (Rutgers). At the Department of Pharmaceutics in New Jersey, He furthered His cancer work by looking at, not only the *Cancer Chemotherapeutic* drugs, but also got deeper into the field of REGULATION OF GENE EXPRESSION. While it was by then recognized that *Acetylation, Methylation,* and *Phosphorylation* are the three main mechanisms by which cancer genes regulate their expression, the MAN OF GOD however, devoted His life into the *elucidation* of PHOSPHORYLATION as the *central mechanism* through which cancer *onco-proteins* are regulated. In talking with Him about this *forte* developed in *phosphorylation*, the MAN OF GOD endears Himself to it as though He was talking about His own baby child.

USING NUCLEAR SCIENCE TO STUDY CANCER GROWTH

In engaging with the MAN OF GOD deeper on the studies of what He calls '*phosphorylation*' as a means of understanding how cancers grow and develop in the human body, that is when you become *the poorer for it*! Nonetheless, I gained the courage to dare Him on a wild *expedition* on this matter of this thing He calls '*phosphorylation*', that I could vividly see from the glow on

Pharmaceutical Research, Vol. 20, No. 9, September 2003 (© 2003) *Research Paper*

Involvement of Nrf2 and JNK1 in the Activation of Antioxidant Responsive Element (ARE) by Chemopreventive Agent Phenethyl Isothiocyanate (PEITC)

Young-Sam Keum,[1] Edward D. Owuor,[1] Bok-Ryang Kim,[1] Rong Hu,[1] and A.-N. Tony Kong[1,2]

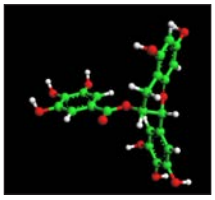
Received February 4, 2003; accepted May 13, 2003

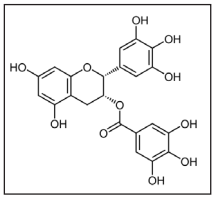
Purpose. Phenethyl isothiocyanate (PEITC) has been of great interest as a promising cancer chemopreventive agent. To better understand its chemopreventive activity, we examined the effect of PEITC on the antioxidant responsive element (ARE), which is an important gene regulatory element of many phase II drug-metabolizing/detoxification enzymes as well as cellular defensive enzymes.
Methods. HeLa cells were transiently transfected with different cDNA plasmids using calcium phosphate precipitation. Subsequently

Brassicaceae) family include broccoli, horseradish, cabbage, cauliflower, and watercress. Cruciferous vegetables are rich in glucosinolates, which can be degraded nonenzymatically by physical factors or enzymatically by myrosinases to isothiocyanates (ITCs) during food preparation, cooking, and chewing (2). Numerous epidemiologic reports showed that consumption of cruciferous vegetables is inversely related to the risk of developing various types of cancer (3). Mechanistic studies have indicated that remarkable chemopreventive activity of ITCs stems from their biological effects on carcinogen metabolism and detoxification. Thus, phenethyl isothiocyanate, the most predominant ingredient among isothiocyanates, has been investigated extensively as a promising chemopreventive compound.

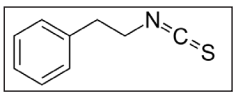
The concept of metabolism modulation as a possible strategy of protection against carcinogenesis originated from the fact that many chemical carcinogens are not chemically reactive *per se* but must undergo bioactivation to electrophiles by certain enzymes (4). Careful observation of drug-metabolizing enzymes led to the recognition of separate enzyme systems, phase I (cytochrome P450s) and phase II drug-metabolizing or detoxifying enzymes. These enzymes are not separate entities but closely linked in action. When exposed

His face, was clearly so beloved to Him, and as a matter of fact seemed so close to His heart! That is when I received the biggest shock of my life, when the MAN OF GOD said it involved NUCLEAR SCIENCE. In the beginning I did not understand, and indeed wondered what *Nuclear Science* has got to do with cancer research, especially that Nuclear Science has embroiled us into such a huge controversy in the political landscape of this world, with Iran versus the West. The PROPHET OF THE LORD went ahead however to give me this lecture of my life, when He said that Phosphorus-32 is a *radioactive isotope* of wild-type Phosphorus. And He went on to say that the Phosphorus-32 nucleus contains 15 protons and 17 neutrons thereby being one more neutron richer than the most common *isotope* contemporary, Phosphorus-31. He further said that Phosphorus-32 only exists in very small quantities in nature and has a short decay time with a half-life of approximately 14 days. And He said it is this short half-life of Phosphorus-32 that has particularly endeared it and made it more of a *desirable darling* to applications in medicine, because it allows Cancer Scientists to track *biochemical* and *metabolic* pathways by radioactively labelling Cellular Molecules such as DNA and proteins. As I sat there marvelled, the MAN OF GOD went on to say to me that the key principle that drove Him to utilize radioactive Phosphorus-32 as an instrument of choice, in studying cancer oncogenes, is because in its decay formula, radioactive Phosphorus-32 releases approximately 1.7MeV of energy through kinetic energy of electrons. When the MAN OF GOD went ahead to even show me the nuclear formula that describes that decay time He was talking about, I decided to copy it word for word and figure for figure on to this article, that the world may get to know the other side of the PROPHET that is so deep and yet had been for some reason either *concealed*, or deliberately *ignored*. And as a commentator who set out to dig these things out, I still believe that these are the hidden marks that truly go a long way to define His stripes, even as He serves the LORD with such a *fierce biblical faithfulness*, the way He does.





Chemical Structure of EGCG

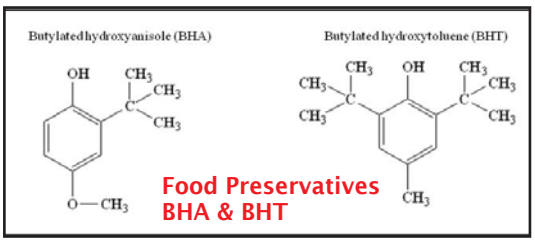


Phenethyle Isothiocyanate

The MAN OF GOD showed me this photo of the way radioactive material used to be packaged and shipped to Him in His Lab. for radioisotope labelling of Cancer Cells.

$$^{32}_{15}P \rightarrow {}^{32}_{16}S^{1+} + e^{-} + \bar{\nu}_e$$

It is this radioactive nuclear kinetic energy *dissipated* in this reaction, that the MAN OF GOD said is so lovely because it can be utilized in a beautiful way to *detect* and *track* the movement of Phosphorus-32 labelled molecules in the cancer cells, through ordinary X-ray technology, again to me I did



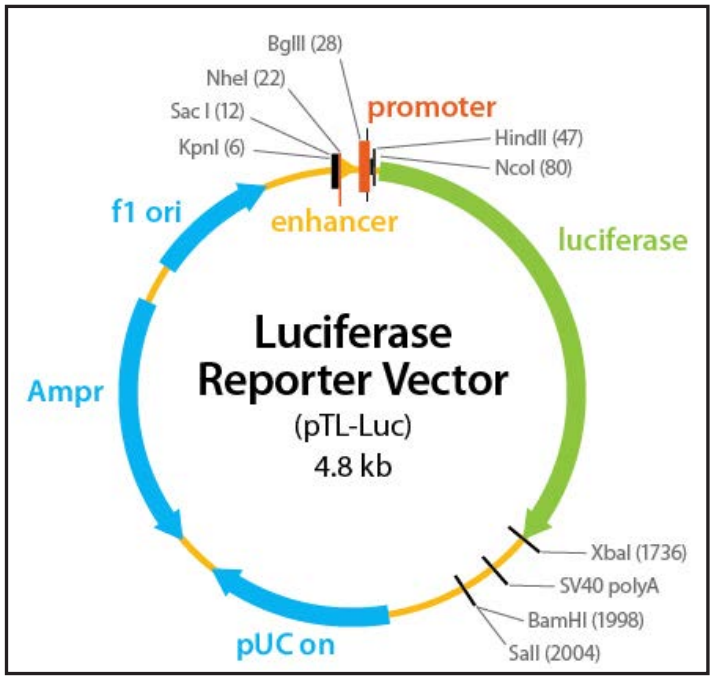
not even see anything lovely about it! Radioactive Phosphorus-32, He said, is a greatly beloved molecule to the Cancer Research Community, because it finds greater use in studying Oncogenes through DNA labelling. The MAN OF GOD further followed this road with me by saying that DNA contains large numbers of Phosphorus in its *phosphodiester* bonds between the bases of the *oligonucleotide* chains. As I thought that I was now finally shocked to my core, then this *relentless* MAN OF GOD went on to say that this technique is also extensively used in *southern blotting*. For me this sounded like rocket science brought on here on earth! However, for the sake of the readers and the peoples of the world, I decided to just continue documenting these profound utterances, that one day it may be known that this was the choice of our GOD.


Luminometer


Standard Reagents For Luciferase Functional Assay For Studying Cancer Gene Induction

Certification by Nuclear Regulatory Commission

Nonetheless, THE PROPHET OF THE LORD went on to say that for Him to be permitted to handle sensitive radioactive material like Phosphorus-32 in the US, He had to get *clearance* and *certification* from the US Government through the NUCLEAR REGULATORY COMMISSION OF THE STATE OF ILLINOIS, and via the Department of Environmental Health and Safety, of the University of Illinois at Chicago, and through its Radiation Safety Program. The MAN OF GOD asserted with great seriousness that only upon His certification by this department, could He be allowed to handle sensitive Radioactive material, and to know how His annual dose limit that He was legally allowed to take in, during His Cancer Research Studies, without exceeding the allowable limit that would cause bodily harm! And also to know how to dispose off their radioactive waste thereof. At this stage of this conversation, I now looked at the MAN OF GOD very differently! Nevertheless, He went on to say that He used to routinely employ this radioactive Phosphorus-32 to constitute His radioactive reaction mix, and then employed it to label the Phosphorus on DNA from different types of carcinomas. In that way, the MAN OF GOD said that He used to fool the cancer cells that they may take up radioactive Phosphorus-32 as their existential inorganic substrate, instead of the wild-type normal inorganic phosphate. The PROPHET OF THE LORD did not spare me even at this greater depth, when He further went on to shock me that after the cancer cell took up the radioactive Phosphorus-32 and incorporated it into its metabolic pathways, then He could track down those signalling pathways using x-ray *autoradiography*. By this, the PROPHET OF THE LORD said that He was then enabled to become the first person to discover the Phosphorylation



domain of PBP, which is a very novel oncologically important Oncogene, as seen in the www.jbc.org publication appended above. Thus, the MAN OF GOD said that He was able to find out which particular sequence and segment of that PBP gene was important for the activation of gene expression in cancer growth and development. In that way, the MAN OF GOD said that upon of the activation domain, Cancer Scientists can then be able to develop a dominant negative PBP activation pathway that the cancers use for growth and spread. What shocked me most though, was when the MAN OF GOD turned around and said that in using radioactive Phosphorus-32 to study the processes of cancer growth, He Himself had to be very careful because this very radioactive Phosphorus-32, is in itself ACTUALLY A CANCER CAUSING AGENT! I must say that, that really stunned me and made my hair stand because I could not understand how anyone could do such a deadly thing to put their lives on the line! Nonetheless, it finally dawned on me to understand much more of what the MAN OF GOD meant at the beginning of this interview, when He said that before the

Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis

Volumes 480–481, 1 September 2001, Pages 231–241

Molecular Mechanisms of Anticarcinogenesis and Antimutagenesis

Signal transduction events elicited by cancer prevention compounds ☆

Ah-Ng Tony Kong, Rong Yu, Vidya Hebbar, Chi Chen, Edward Owuor, Rong Hu, Rachel Ee, Sandhya Mandlekar[1]

Department of Pharmaceutics and Pharmacodynamics, Center for Pharmaceutical Biotechnology, MC 870, College of Pharmacy, University of Illinois at Chicago, 900 S. Ashland Ave, Chicago, IL 60607, USA

Received 17 October 2000, Revised 31 January 2001, Accepted 1 February 2001, Available online 9 August 2001

Abstract

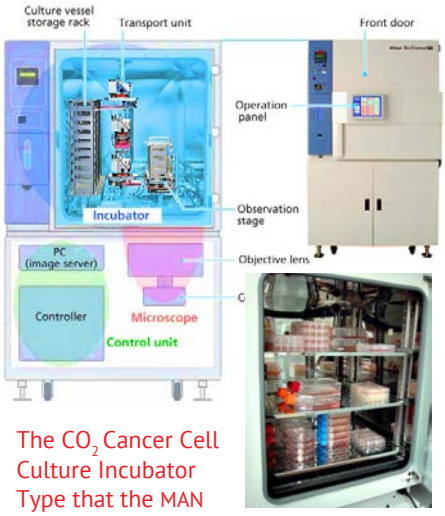
Many chemopreventive agents have been shown to modulate gene expression including induction of phase II detoxifying enzymes, such as glutathione S-transferases (GST) and quinone reductases (QR). Induction of phase II enzymes in general leads to protection of cells/tissues against exogenous and/or endogenous carcinogenic intermediates. The antioxidant or electrophile response element (ARE/EpRE) found at the 5′-flanking region of these phase II genes may play important role in mediating their induction by xenobiotics including chemopreventive agents. Members of the basic leucine zipper (bZIP) transcription factor, Nrf2 which heterodimerizes with Maf G/K, are found to bind to the ARE, and transcriptionally-activated ARE. Recently, we showed that the mitogen-activated protein kinases (MAPK) were activated by phase II gene inducers such as phenolic antioxidant butylated hydroxyanisol (BHA) and isothiocyanate sulforaphane (SUL), and involved in the transcription activation of ARE-mediated reporter gene. Transfection studies with wild-type and dominant negative mutants of Nrf2 and MAPK showed synergistic response during co-transfection as well as to phase II gene inducers. However, increasing the concentrations of these compounds such as BHA, the activities of cell death signaling molecules, caspases, were stimulated and resulted in apoptotic cell death. At these concentrations, BHA stimulated loss of mitochondrial membrane potential, cytochrome c release, and activation of caspase 3, 8 and 9 preceding apoptosis. Further increase in concentrations led to rapid cell necrosis. A model is proposed for BHA and SUL, in that at low concentrations, these potential chemopreventive agents may modulate MAPK pathway leading to transcription activation of Nrf2 and ARE with subsequent induction of cellular defensive enzymes including phase II detoxifying enzymes as well as other defensive genes, which may protect the cells against cellular injury, which is a homeostatic response. At higher concentrations, these agents may activate the caspase pathways, leading to apoptosis, a potential beneficial effect if occurs at preneoplastic/neoplastic tissues, but a potential cytotoxic response if occurs in normal tissues. On the other hand, some phenolic compounds such as resveratrol inhibits TPA- or UV-induced AP-1-mediated activity through the inhibition of c-Src non-receptor tyrosine kinase and MAPK pathways. It is possible that in proliferating or stimulated cells, these chemopreventive compounds may block proliferation by inhibiting these signaling kinases, whereas in non-proliferating or quiescent cells, some of these compounds may activate these signaling kinases leading to gene expression of cellular defensive enzymes such as phase II detoxifying enzymes. The studies of these and other signaling pathways may yield insights into the development of potential chemopreventive compounds.

Abbreviations

BHA, 2(3)-*tert*-butyl-4-hydroxyanisole; *t*BHQ, *tert*-butyl-hydroquinone; GTP, green tea polyphenols; EGCG (−)-epigallocatechin-3-gallate; EGC (−)-epigallocatechin; TAM, tamoxifen; QUE, quercetin; PMITC, phenylmethyl isothiocyanate; PEITC, phenethyl isothiocyanate; SUL, sulforaphane; MAPK, mitogen-activated protein kinase; ERK2, extracellular signal-regulated protein kinase 2; JNK1, c-Jun N-terminal kinase 1; MAPKKK, MAP kinase kinase kinase; MEKK1, MAPK/extracellular signal-regulated kinase kinase kinase 1; TAK1, transforming growth factor-β-activated kinase 1; ASK1, apoptosis signal-regulating kinase 1; MKK, MAPK kinase; MEK, MAPK/extracellular signal-regulated kinase kinase; NFκB, nuclear factor κB; AP-1, activated protein 1; PKC, protein kinase C; Hog1, high osmolarity glycerol response-1; Nrf2, NF-E2-related factor 2; EGF, epidermal growth factor; PDGF, platelet-derived growth factor; P13K, phosphoinositide 3-kinase; PKB, protein kinase B; DAG, diacylglycerol; ICE/Ced-3; Interleukin-1β (IL-1β) converting enzyme/caernohabditis elegans *ced-3* gene; Cyto c, cytochrome c; GST, glutathione S-transferases; NQO, DT-diaphorase or NAD(P)H:quinone oxidoreductase or NAD(P)H:menadione reductase; HO-1, hemeoxygenase-1; ARE/EpRE, antioxidant response element/electrophile response element

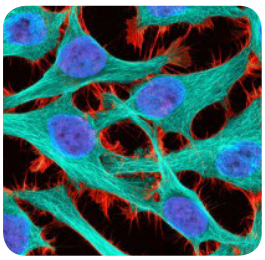
LORD called Him, He had AS A MATTER OF FACT GIVEN HIS ENTIRE LIFE TO FINDING THE CURE FOR CANCER. By surveying scientific literature on this radioactive Phosophorus-32 that the MAN OF GOD was talking about, is when I realized that there is actually no way one would voluntarily expose themselves to such grim danger of deadly radioactive Phosphorus-32 experiments that actually cause cancer themselves, for the sake of studying cancer! Unless you have REALLY GIVEN YOUR LIFE TO IT! This really threw me aback! And talk about giving one's life to it, I can now clearly see that indeed He had given His life total to Cancer Research. The MAN OF GOD did not stop here, but went on to further say that it was during then, that He also worked deeper into the role of *Nuclear Transcription Factors* as major gene switches that control the expression of cancer-related genes. The gravity of His work on *Transcription Factors* He said, arose from the fact that studies of Transcriptional regulation have today become a very lucrative branch of *drug discovery* hence earning the central focus of almost all major Pharmaceutical Giants globally. In the list He handed to me, I found out that the *Transcription Factors* that the PROPHET OF THE LORD examined included *c-Jun, p38* and the *NUCLEAR RELATED FACTOR-2* (Nrf-2). In examining these *Transcription Factors*, the MAN OF GOD said that c-Jun is a Cellular Stress-related factor that responds to oxidative stress by reactive oxygen species (ROS) which cause cancer, thereby qualifying this Transcription Factor for proper indepth studies for mitigation. He went to elaborate how He squarely narrowed down and focused on the Nrf-2 *Transcription Factor* which turned out to be the *Nuclear Master Switch* that controls the expression and activation of all the anti-oxidant regulated defensive anti-cancer genes in the human body. While describing this, the MAN OF GOD did not forget to emphasize to me that this He discovered to be the main way in which the human body switches on its defensive antioxidant *genes* and

enzymes. Such defensive *genes* that He elaborated to me included *Haeme oxygenase-1(HO-1),* and *Glutathione-S-Transferase (GST)* among others. In order to facilitate His research on the potency of any of the cancer-chemotheraputic and chemo-preventive compounds, the MAN OF GOD told me that He had to employ a robust functional assay which essentially involved *cloning* the respective genes onto a plasmid vector that contained the *Luciferase* Reporter gene.



The CO_2 Cancer Cell Culture Incubator Type that the MAN OF GOD used to grow His cancer cells in Petri dishes at 36.9 - 37° C

In order to incorporate all these MAP-K genes onto the cancer cell for gene expression, the MAN OF GOD had to utilize the Luciferase Reporter Gene Construct together with its respective gene promoter region. This construct became a very powerful platform for the MAN OF GOD to verify the expression of His Kinase genes of interest because, by simple transfection studies He could achieve a robust gene transfer into the cancer cells and monitor their consequent expression. The Luciferase reporter gene system that the MAN OF GOD used in His functional assays, literally involved exploiting the *firefly* gene that the *firefly* uses at night when it flies in the darkness to illuminate its path. In that system, the *firefly* gene is extracted from the *firefly* and used in basic *cloning* procedures to build a Luciferase gene construct which contain the gene of the firefly within the bacterial plasmid. So as to perform a selection of the positives verses the negatives of the gene construct, the MAN OF GOD emphasized that He employed simple bacterial plasmids that HE grew in specific bacteria for amplification, and then performed simple studies using antibiotic selection in order to find out which cells had successfully incorporated the right gene at the right sequence. It is these Luciferase gene constructs that the MAN OF GOD used in co-transfection with MAP-K genes into cancer cells, and monitored their consequent gene expression profiles within those cancer cells through normal cell lysis and luminescence studies by the use of a computerised *Luminometer*, which can detect the amount of *luminescence*, against a blank control with only the buffer solution. In that way, the MAN OF GOD was able to examine the fold inductions of gene expressions within the cancer cells and then model an intervention strategy to shut down important gene expression profiles that sustain cancer cells. This shutting down of genes He Said, is what constitutes drug discovery and design, especially when He would design a gene construct that contains the DOMINANT NEGATIVE protein which when administered blocks and shuts down the pathways of oncogenesis and tumorigenesis.



The Cervical Carcinoma cells that the MAN OF GOD studied were supplied by The American Cell Type Culture. He used the HeLa Cervical Cancer Model.

CANCER CHEMOPREVENTION

The PROPHET OF THE LORD went on and on, with this deep science of finding a cure for cancer. At this point, it became impossible for me to stop Him any longer as He seemed to be in another world as He described to me this thing that now clearly dawned on me as His forte! In that way, He went on to say that there are 2 types of drugs namely, *phase I* drugs and *phase I I* drugs, and yet He chose to focus on human *liver-phase 2* drugs that are involved in body defence. In His narrative, He said, that is when He became very zealous about studying the role of Cancer Chemo-prevention compounds as a means of improving public health by stopping the onset of cancers before they develop into the human body. This caused Him to directly become interested in understanding why different populations of Americans *verses* the Chinese have different prevalence rates for different cancers. He went on to underscore that He had developed a particular interest to find out exactly why the colorectal cancers would be more prevalent among the Americans, than among the Chinese populations. He said that this caused Him to become directly interested and engaged in the differences in eating *habits* and *lifestyles* among different populations, and how such differences in *lifestyle* patterns, can *predispose* different populations to particular types of cancers. In His description, it comes out clearly that it was during this time, the MAN OF GOD became interested in researching why eating a lot of vegetables like *broccoli*, and drinking a lot of *green tea*, together with exercising, protected certain Chinese people from certain types of cancers. Working together with other top notch *Cancer Professors*, the MAN OF GOD became part of the team that identified that particular vegetables like *broccoli* contained important class of chemicals called ISOTHIOCYANATES, and more specifically the chemical family of *PHENETHYL ISOTHIOCYANATE (PEITC)*. This is the part of the conversation that became much more interesting to me, because He said that the people who eat a lot of Broccoli accumulate significant amounts of PEITC that enables them to receive protection from cancer. The PROPHET OF THE LORD then proceeded to walk me through a process in which He went ahead and alone to take on this PEITC chemical and conduct a thorough indepth study into how this chemical achieves its cancer chemo-

Pharmaceutical Research, Vol. 20, No. 9, September 2003 (© 2003) *Research Paper*

Involvement of Nrf2 and JNK1 in the Activation of Antioxidant Responsive Element (ARE) by Chemopreventive Agent Phenethyl Isothiocyanate (PEITC)

Young-Sam Keum,[1] Edward D. Owuor,[1] Bok-Ryang Kim,[1] Rong Hu,[1] and A.-N. Tony Kong[1,2]

Received February 4, 2003; accepted May 13, 2003

Purpose. Phenethyl isothiocyanate (PEITC) has been of great interest as a promising cancer chemopreventive agent. To better understand its chemopreventive activity, we examined the effect of PEITC on the antioxidant responsive element (ARE), which is an important gene regulatory element of many phase II drug-metabolizing/detoxification enzymes as well as cellular defensive enzymes.
Methods. HeLa cells were transiently transfected with different cDNA plasmids using calcium phosphate precipitation. Subsequently, the cells were maintained in fresh media, and various concentrations of PEITC were added to the transfected cells. After harvesting and lysing of the cells, ARE-luciferase reporter gene activity was measured and normalized against β-galactosidase activity.
Results. Treatments of HeLa cells with PEITC transiently stimulated ARE-reporter gene expressions in a dose-dependent manner. Overexpression of wild-type NF-E2 related factor-2 (Nrf2) dramatically increased ARE-reporter gene expression in a dose-dependent manner. Similar effects were seen when wild-type c-Jun N-terminal kinase 1 (JNK1) was transfected, although the transactivating potential of JNK1 was much less than that of Nrf2. Cotransfection of Nrf2 and JNK1 showed additional enhancement of ARE reporter gene expression, implying that JNK1 might be an upstream activator of Nrf2. To support this, overexpression of dominant-negative JNK1 suppressed Nrf2-induced ARE reporter gene expression in a dose-dependent manner. When PEITC was added, slight enhancement of ARE reporter gene expression was observed in either Nrf2- or JNK1-transfected cells. Finally, ARE reporter activity induced by PEITC was substantially attenuated by transfection of either dominant-negative mutant of Nrf2 or dominant-negative mutant of JNK1.
Conclusion. Taken together, these data suggest that JNK1 acts as an upstream activator of Nrf2 and that PEITC activates ARE-mediated phase II drug metabolism gene expressions via the JNK1- and Nrf2-dependent pathways.

KEY WORDS: chemoprevention; isothiocyanate (ITC); phenethyl isothiocyanates (PEITC); antioxidant response element (ARE); Nrf2; JNK1; signal transduction.

Brassicaceae) family include broccoli, horseradish, cabbage, cauliflower, and watercress. Cruciferous vegetables are rich in glucosinolates, which can be degraded nonenzymatically by physical factors or enzymatically by myrosinases to isothiocyanates (ITCs) during food preparation, cooking, and chewing (2). Numerous epidemiologic reports showed that consumption of cruciferous vegetables is inversely related to the risk of developing various types of cancer (3). Mechanistic studies have indicated that remarkable chemopreventive activity of ITCs stems from their biological effects on carcinogen metabolism and detoxification. Thus, phenethyl isothiocyanate, the most predominant ingredient among isothiocyanates, has been investigated extensively as a promising chemopreventive compound.

The concept of metabolism modulation as a possible strategy of protection against carcinogenesis originated from the fact that many chemical carcinogens are not chemically reactive *per se* but must undergo bioactivation to electrophiles by certain enzymes (4). Careful observation of drug-metabolizing enzymes led to the recognition of separate enzyme systems, phase I (cytochrome P450s) and phase II drug-metabolizing or detoxifying enzymes. These enzymes are not separate entities but closely linked in action. When exposed to chemical carcinogens, phase I enzymes convert potential carcinogens by oxidation or reduction. Phase II enzymes then promote the conjugation of phase I products with endogenous cofactors such as glutathione (by glutathione *S*-transferase; GST) and glucuronic acid (by UDP-glucuronosyltransferases; UGT), resulting in more water-soluble products, which can be easily excreted.

Many investigators have shown that induction of several phase II and cellular defensive enzymes is under the transcriptional control of antioxidant responsive element (ARE) (5). The promoters of many of these genes, including GST, NAD(P)H: quinone oxidoreductase (NQO), γ–glutamylcysteine synthetase (γ-GCS), and heme oxygenase I (HO-1), indeed possess the ARE DNA sequence. The core sequence of ARE as obtained by mutational analyses is GTGACNNNGC (6,7). This sequence bears a resemblance to the nuclear factor E2 (NF-E2) consensus sequence, which is positively controlled by a transcriptional factor, NF-E2 related factor 2 (Nrf2). There is much evidence to show that Nrf2 is a key transcription factor of ARE activation. First, many of Nrf2 target genes encode proteins that play an important role in the adaptive response to oxidative stress with association of other cofactors, such as Maf family proteins (8). Second, exogenous induction of either wild-type or dominant-negative Nrf2 can positively or negatively regulate ARE expression

preventive role in the human body. The MAN OF GOD elaborated to me that moment when He discovered the *signal transduction* pathways that PEITC exploits in order to induce cancer chemoprevention among those who observe that type of *lifestyle*. And as though to indeed confirm and underscore to me that what He was saying was as a matter of fact TRUE, I found out that these novel Cancer Research works were indeed published together with His Ph.D. Student, and other colleague Professors, in Prestigious *Journals*, including the work on PEITC published in the revered *Journal For Pharmaceutical Research* that I appended as incontrovertible proof in this article. At this point, as I sat there talking to the MAN OF GOD, I was totally mesmerised because all this indepth description of His work TRULY HAD AN INDISPUTABLE, UNDENIABLE AND UNMISTAKABLE EVIDENCE THROUGH PEER REVIEW TOP NOTCH WORLD CLASS CANCER RESEARCH JOURNAL PUBLICATIONS WITH HIS NAMES ON. And it indeed amazed me that those journals are available free of charge at the website of the National Library of Medicine of the United States of America, called Pubmed. Moreover, as I was sitting there in surprise, the MAN

CANCER INSTITUTE OF NEW JERSEY (CINJ)

OF GOD simply went on to elaborate further that for regular *green tea* drinkers, a major chemical component called GREEN TEA POLYPHENOLS of the class known as EPIGALLOCATECHIN-3-GALLET (EGCG), was found to be of great benefit in protecting *green tea* drinkers. THE PROPHET OF THE LORD then became interested in the *signal transduction* mechanisms, and the *biochemical pathways* that are induced in the human body by these chemicals. That is what led Him to work on the *biochemical signalling pathways* that induce the expression of Phase II drug metabolising *antioxidant* and *detoxification* genes in the human body. While underscoring that cancer chemoprevention was key in His work, the MAN OF GOD THE PROPHET said that *detoxification* and *excretion* serve as the main mechanisms by which the human body fights environmental insults like exposure to mercury and cigarette smoke that cause cancer. Other environmental *toxicants* that became of interest to the MAN OF GOD included exposure to *Benzene* from motor vehicle *exhaust fumes*, and other DNA-altering chemical pollutants such as *cigarette smoke*, *ammonia, selenium,* and *molybdenum isotope* that today lace-up our environment. That is when the PROPHET OF THE LORD also described how He got interested in studying how *BHA & BHT* which are commonly used as *preservatives* in canned foods, cause cancer. Furthermore, He also got interested in studying the role of *Mono Sodium Glutamate (MSG)* which is found in lots of our gravy spices, and how they cause cancer. The role of these environmental chemicals in igniting *tumorigenesis, oncogenesis* and *carcinogenesis* in the human body and the relevant *mitigation prevention mechanisms* in the body, then became His *forte* and life-long commitment. Because of the novelty of such work, it caught the interest of the US Media, and were consequently covered by the *New Jersey Channel 12 State TV News,* and the *New Jersey Star Ledger Newspaper* which came to His laboratory and interviewed Him on the broad spectrum of His *findings* and *discoveries*, and their implications to

Research Article

Induction of xenobiotic enzymes by the map kinase pathway and the antioxidant or electrophile response element (ARE/EpRE)

2001, Vol. 33, No. 3-4 , Pages 255-271

A.-N. Tony Kong, Edward Owuor, Rong Yu, Vidya Hebbar, Chi Chen, Rong Hu, and Sandhya Mandlekar

Center for Pharmaceutical Biotechnology, Department of Pharmaceutics and Pharmacodynamics, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois, U.S.A.

Department of Pharmaceutics, College of Pharmacy, Rutgers University, Environmental and Occupational Health Sciences Institute, 160 Frelinghuysen Road, Room 228, Piscataway, NJ, 08854, U.S.A.

Department of Drug Metabolism and Pharmacokinetics, DuPont Pharmaceutical Company, Newark, Delaware, U.S.A.

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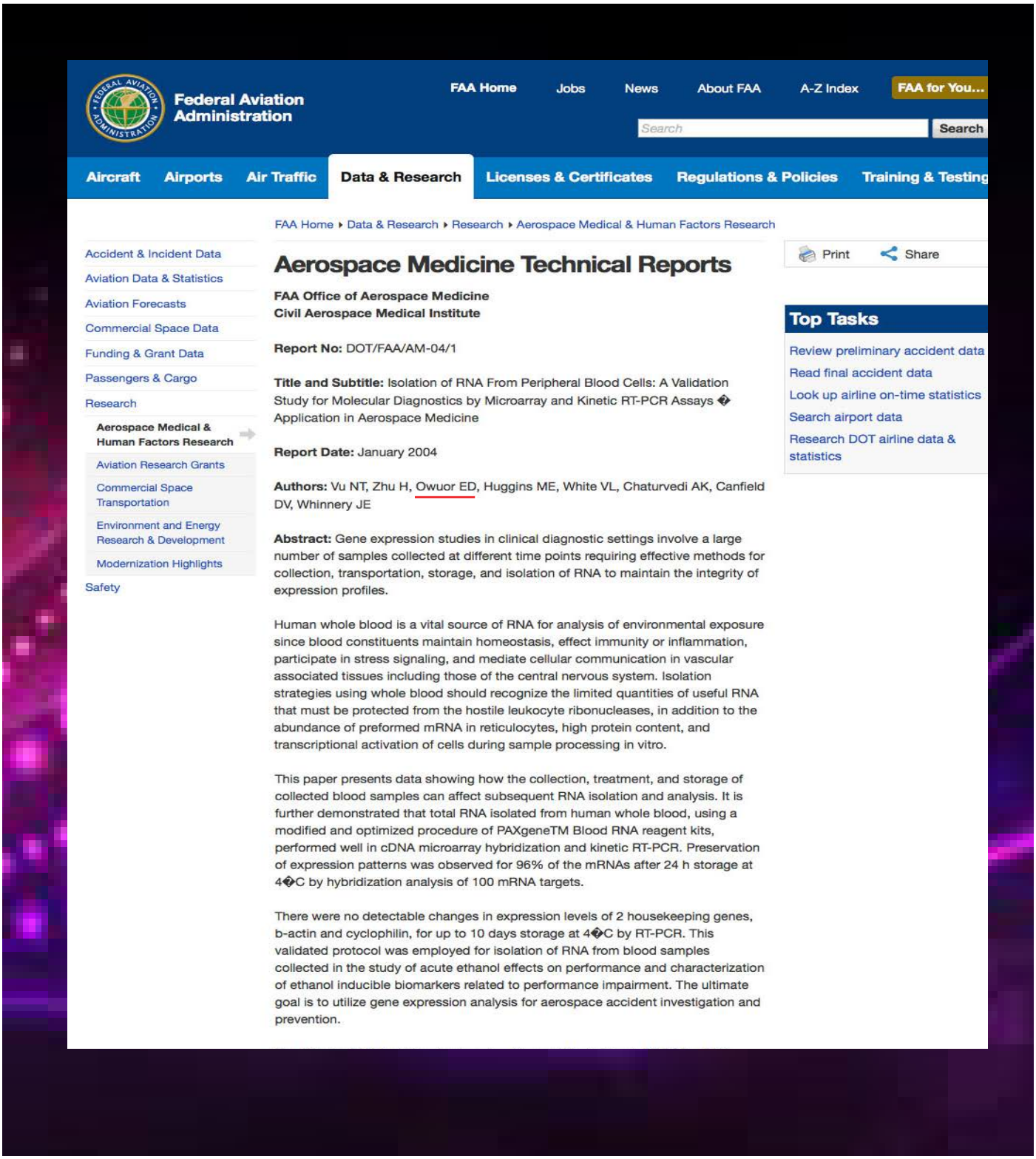
‡This paper was referred by Dr. F. P. Guengerich, Vanderbilt University, Nashville, TN 37232.

Cellular responses to xenobiotic-induced stress can signal proliferation, differentiation, homeostasis, apoptosis, or necrosis. To better understand the underlying molecular mechanisms after exposure to xenobiotics or drugs, we studied the signal transduction pathways, the mitogen-activated protein kinase (MAPK), and the basic leucine zipper transcription factor Nrf2, activated by different agents in the induction of Phase II drug metabolizing enzymes (DMEs). The MAPKs, characterized as proline-directed serine/threonine kinases, are essential components of signaling pathways that convert various extracellular signals into intracellular responses through serial phosphorylation cascades. Once activated, MAPKs can phosphorylate many transcription factors, such as c-Jun, ATF-2, and ultimately lead to changes in gene expression. Two classes of Phase II gene inducers, which are also cancer chemopreventive agents, were studied: (1) the phenolic antioxidants, namely butylated hydroxyanisole (BHA) and its active de-methylated metabolite *t*-butylhydroquinone (*t*BHQ), and phenolic flavonoids such as green tea polyphenols (GTP) and (−)-epigallocatechin-3-gallate (EGCG); and (2) the naturally occurring isothiocyanates, namely phenethyl isothiocyanate (PEITC), and sulforaphane. BHA and *t*BHQ are both well-known phenolic antioxidants used as food preservatives, and strongly activate c-Jun N-terminal kinase 1 (JNK1), extracellular signal-regulated protein kinase 2 (ERK2), or p38, in a time- and dose-dependent fashion. Free radical scavengers *N*-acetyl-L-cysteine (NAC), or glutathione (GSH), inhibited ERK2 activation and, to a much lesser extent, JNK1 activation by BHA/tBHQ, implicating the role of oxidative stress. Under conditions where MAPKs were activated, BHA or GTP also activated ARE/EpRE (antioxidant/electrophile response element), with the induction of Phase II genes such as NQO. Transfection studies with various cDNAs encoding wild-type or dominant-negative mutants of MAPKs and/or transcription factor Nrf2, substantially modulated ARE-mediated luciferase reporter activity in the presence or absence of phenolic compounds. Other phytochemicals including PEITC, and sulforaphane, also differentially regulated the activities of MAPKs, Nrf2, and ARE-mediated luciferase reporter gene activity and Phase II enzyme induction. A model is proposed where these xenobiotics (BHA, *t*BHQ, GTP, EGCG, PEITC, sulforaphane) activate the MAPK pathway via an electrophilic-mediated stress response, leading to the transcription activation of Nrf2/Maf heterodimers on ARE/EpRE enhancers, with the subsequent induction of cellular defense/detoxifying genes including Phase II DMEs, which may protect the cells against toxic environmental insults and thereby enhance cell survival. The studies of these signaling pathways may yield insights into the fate of cells upon exposure to xenobiotics.

Keywords

MAPK, Signal transduction, Phase II drug metabolizing enzymes, Nrf2;Chemopreventive agents



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Aerospace Medicine Technical Reports

FAA Office of Aerospace Medicine
Civil Aerospace Medical Institute

Report No: DOT/FAA/AM-04/1

Title and Subtitle: Isolation of RNA From Peripheral Blood Cells: A Validation Study for Molecular Diagnostics by Microarray and Kinetic RT-PCR Assays Application in Aerospace Medicine

Report Date: January 2004

Authors: Vu NT, Zhu H, Owuor ED, Huggins ME, White VL, Chaturvedi AK, Canfield DV, Whinnery JE

Abstract: Gene expression studies in clinical diagnostic settings involve a large number of samples collected at different time points requiring effective methods for collection, transportation, storage, and isolation of RNA to maintain the integrity of expression profiles.

Human whole blood is a vital source of RNA for analysis of environmental exposure since blood constituents maintain homeostasis, effect immunity or inflammation, participate in stress signaling, and mediate cellular communication in vascular associated tissues including those of the central nervous system. Isolation strategies using whole blood should recognize the limited quantities of useful RNA that must be protected from the hostile leukocyte ribonucleases, in addition to the abundance of preformed mRNA in reticulocytes, high protein content, and transcriptional activation of cells during sample processing in vitro.

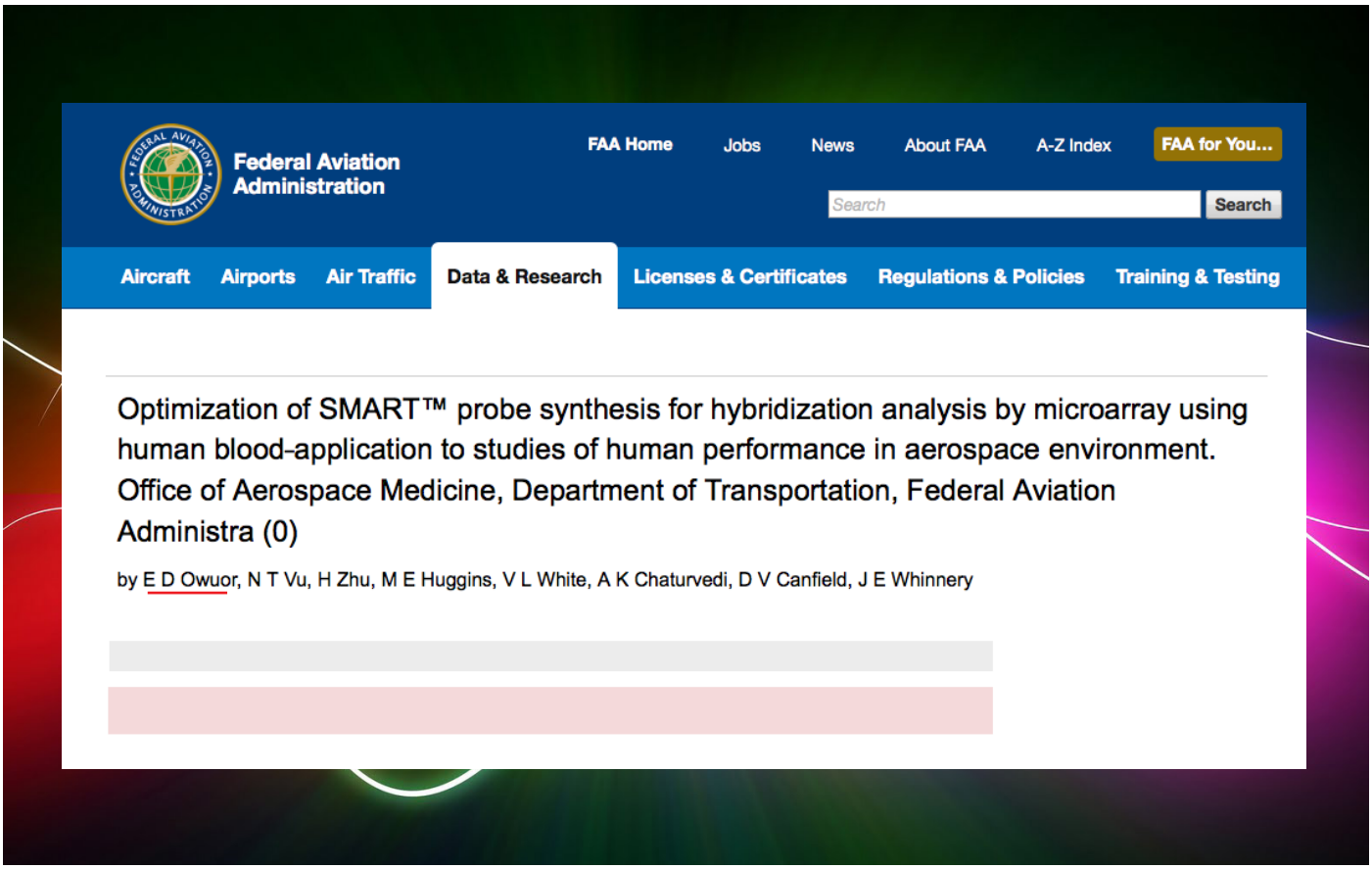
This paper presents data showing how the collection, treatment, and storage of collected blood samples can affect subsequent RNA isolation and analysis. It is further demonstrated that total RNA isolated from human whole blood, using a modified and optimized procedure of PAXgeneTM Blood RNA reagent kits, performed well in cDNA microarray hybridization and kinetic RT-PCR. Preservation of expression patterns was observed for 96% of the mRNAs after 24 h storage at 4C by hybridization analysis of 100 mRNA targets.

There were no detectable changes in expression levels of 2 housekeeping genes, b-actin and cyclophilin, for up to 10 days storage at 4C by RT-PCR. This validated protocol was employed for isolation of RNA from blood samples collected in the study of acute ethanol effects on performance and characterization of ethanol inducible biomarkers related to performance impairment. The ultimate goal is to utilize gene expression analysis for aerospace accident investigation and prevention.

Top Tasks

- Review preliminary accident data
- Read final accident data
- Look up airline on-time statistics
- Search airport data
- Research DOT airline data & statistics

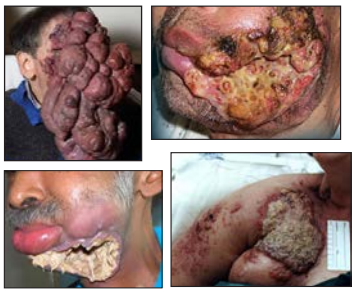
public health. Throughout all this time, the MAN OF GOD was an established member of the American Association for Pharmaceutical Scientists (AAPS), in whose annual conferences, He presented His research works. I found out that the MAN OF GOD also gave some serious conferences on His findings at various Pharmaceutical Companies such as at the Global Giant Merck Pharmaceuticals, at their headquarters in West Point Pennsylvania. At Merck He gave the lecture on His findings and discovery of Extracellular Regulated Kinase-5 (Erk-5 signalling and the cross-talk between what He called the Oncogene MKK6 and the p38 cell death pathway, and the implications of that cross-talk on drug resistance by various types of cancers. I found out that the MAN OF GOD also indeed collaborated with many other pharmaceutical giants who often invited Him to share in the findings of His novel work in *Cancer Research* for *Drug Design* and *Discovery*. In that way, He also collaborated with *Centocor Pharmaceutical Company* that was based at Marvin Valley Pennsylvania, with whom He co-authored the paper on *QUINACRINE*. During all that time, the MAN OF GOD THE PROPHET also further published that work in the prestigious Journal of the Korean Pharmaceutical Society. ■



CANCER INSTITUTE OF NEW JERSEY

Robert Wood Johnson Medical School

The *Robert Wood Johnson Medical School* in conjunction with the *University of Medicine and Dentistry of New Jersey (UMDNJ),* run a very *prestigious* cancer centre called the *Cancer Institute of New Jersey (CINJ).* As a *Centre of Excellence*, the *Cancer Institute of New Jersey* hosts several top notch Faculty Professors and Cancer Specialists of different disciplines, thereby encompassing the complete spectrum of *Cancer Research, Treatment*, *Education* & *Prevention*. CINJ is constituted by several divisions that include among others, the Division of Medicine and the Division of Surgical Oncology, to mention. It was in one of these *prestigious* divisions, that the MAN OF GOD was appointed, having been *approached* and *recruited* from The Environmental & Occupational Health Sciences Institute (EOHSI), by the Founder Professor of the Cancer Institute himself. At that time, the MAN OF GOD and the Founding Professor of the Cancer Institute of New Jersey had their offices adjacent to one another on the same floor of the Environmental and Occupational Health Sciences Institute. Having perused through the MAN OF GOD'S publication and became familiar with His research work, the Founding Professor of the Cancer Institute of New Jersey approached the MAN OF GOD who was at that time His next door neighbour office-wise. Owing to His academic credentials and publications, the MAN OF GOD was consequently appointed to the Department of Surgery at the Robert Wood Johnson Medical School, and more specifically within the Division of Surgical Oncology of the Cancer Institute of New Jersey. The MAN OF GOD was appointed as a *Research Teaching Specialist-III (RTS-III),* which involved co-ordinating *Cancer Research* & *Training* several MD-Ph.D Surgeons that were involved in *Oncological Research*. These were *Surgeons* who had risen in their medical education to the Ph.D level, hence in addition to performing surgery and patient care, they were *required* to get involved in ground-breaking cancer research. Since the surgical theatres offer wonderful samples of *fresh human tumors* for research, this was a brilliant opportunity to do ground breaking Cancer Research. Those Surgeons were also required to write *research grants* to the *National Cancer Institute (NCI),* and the *National Institute of Health (NIH).* That is where the MAN OF GOD'S expertise in handling various *sophisticated* techniques in cancer research such as *Signal Transduction Analysis*, *Protein Assays, Oncoprotein Networks, cDNA Microarray platforms, Pharmacokinetics, Pharmacodynamics,* and *Toxicology*, came in very handy. At the Cancer Institute, the MAN OF GOD brought on board these *techniques* in order to *strengthen* the *understanding* of the processes that lead to *TUMOUR ANGIOGENESIS*. This is the mechanism



Horrible Cancers

by which cancers *grow* and *spread* in the human body. Unveiling this process on *tumor angiogenesis* also held a very important key that would open the door into understanding the phenomenon of *Multi-Drug Resistance* (MDR) and *metastasis* in cancers. This process is the one responsible for mortality among cancer patients despite their being under prescription *therapeutic* regimes. Tumor angiogenesis is the main process by which cancers undertake different *biochemical signalling pathways* other than those conventional pathways that are targeted by drugs, thereby *evading* medication. This bore a very critical research undertaking owing to the fact that several cancers today exploit this process of *TUMOUR ANGIOGENESIS* to evade *drug therapy*, and lead to the death of many patients. According to the MAN OF GOD, this is what has *exponentially* increased cancer-related deaths not only in the United States of America, but world over. Therefore, the process of *TUMOUR ANGIOGENESIS* merited a full-fledged *research* study on its own accord since it held the *key* to a very important *gateway* into understanding cancers. This phenomenon in which cancers can *switch* their genes back and forth to evade *apoptosis* (self-suicide), became a very important target in cancer-related mortality. Central in this research was the finding that two major *gene-switches* control *CANCER ANGIOGENESIS* in the human body. The two genes that the MAN OF GOD became interested in, were *Vascular Endothelial Growth Factor a (VEGFa),* and *Vascular Endothelial Growth Factor b (VEGFb).* It was at the *height* of this Cancer Research & Teaching at the *Cancer Institute* that the MAN OF GOD THE PROPHET became deeply interested in unveiling how the *vascular endothelial growth* factor genes produce special protein *chemical messengers* that are released from the cancer cells themselves, into the surrounding tissue. These *chemical messengers* are the ones that are sent out by the cancer cells to the normal neighbouring cells, to command such normal body tissues to undergo *malignant* transformation. These *chemical messengers* of *VEGF* hence essentially command the surrounding normal cells in the human body to *tubulate* and *grow* as *blood vessels* towards the cancer cells. The *tubulated* cells hence begin to *migrate* towards the cancer cells, while *channelling* nutrients that are intended to *feed* the cancer cells. Among the nutrients that were identified as essential for the growth of cancer cells, was *sucrose.* Many cancers heavily depend on *sucrose* as their major staple *diet* which they crave for *rapid* growth. This is just how the cancer cells that the MAN OF GOD THE PROPHET targeted, *grow* and *multiply* uncontrollably to become larger and achieve maximum *tumorigenesis.* As a result of this study, the PROPHET OF THE LORD became so much *engrossed* in trying to understand the processes of *transcriptional* regulation of *gene expression* by these two major gene switches. That is just how far the MAN OF GOD *delved* deep into the vast ocean of cancer *drug design* and *discovery.* ■

THROAT CANCER HEALED WITHOUT SURGERY OR CHEMOTHERAPY

FRANCIS ODUOR

Before Healing

After Healing

KISUMU REVIVAL MEETING

When THE MAN OF GOD was in academia, HE spent all HIS life looking for a cure for cancer. The complex and sophisticated procedures and research HE undertook to study and find a cure for cancer, are clearly well elaborated above. And during all that time, as the LORD was calling Him, He kept running away from THE LORD. Now, the humour of it all, is that when HE said YES to the calling of the LORD, and accepted to go serve the LORD, GOD ALMIGHTY IS NOW HEALING THE VERY CANCERS THE MAN OF GOD WAS TOILING TO FIND THEIR CURE. Its amazing that the MAN OF GOD kept using this excuse of looking for a cure for cancer as THE REASON NOT TO ACCEPT GOD'S CALLING. NOW THE LORD HAS INDEED ONCE MORE PROVED TO THE WORLD THAT HE IS THE KING OF ALL KNOWLEDGE EVEN IN MEDICINE and no one can ever shun HIM for the sake of vain human wisdom.

Francis Oduor from Siaya had suffered Chronic Throat Cancer for many years and had resigned to committing suicide, because no medication seemed to work and nothing would save his life anymore, at least based on what the Doctors had told him. The cancer had eaten deep into his throat and also spread and knocked out his right eye. When a member of the Ministry of Repentance visited him and shared the Mighty Healing of the LORD that normally take place in the Revival Meetings of the MIGHTY PROPHET OF THE LORD, it was then that Francis decided to give it a try and attend the Kisumu Revival Meeting as a last ditch effort. And as soon as the MAN OF GOD arrived at the stadium, tremendous POWER hit Francis and he was slain by the Holy Spirit and lay on the ground for many hours. Upon waking up, he realized that he was now strong enough and no pain any more. Days later, he noticed that the cancer had drastically reduced in size by itself, until it finally totally dissolved. From that day on, his right eye was properly healed and sealed and to this day, he lives free from cancer and MAY THE LORD GOD BE ETERNALLY GLORIFIED!

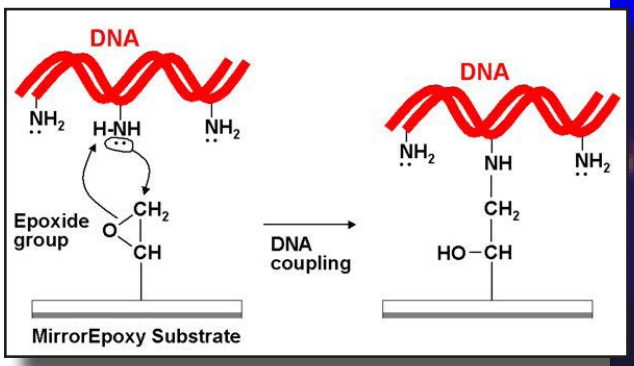
CIVIL AEROSPACE MEDICAL INSTITUTE (CAMI)

FORENSIC TOXICOLOGY & AIRCRAFT ACCIDENTS

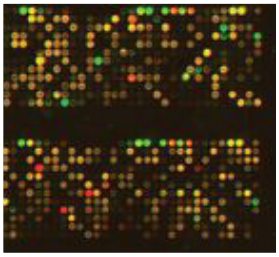
WHEN I THOUGHT THAT the intense knowledge on cancer research studies that the MAN OF GOD just downloaded had struck me down, then came yet another profound depth of how much the MAN OF GOD delved into a totally different world of Forensic Toxicology and Aircraft Accidents. Going through this MAN OF GOD'S extensive resume, all one can pick out is none other than to watch out everytime the LORD Calls somebody. If this is the same man that the LORD GOD was pursuing to take up HIS Calling, and yet His academic endeavours appears to be endless, then this serves as a serious lesson to us all that when the LORD Calls somebody, they ought to be careful on what the world offers. The picture that emerges out of this deep involvement in science by this MAN OF GOD is that of a stiff neck-to-neck competition between the world on one hand offering all flamboyant careers, and the LORD on the other hand, pursuing a serious divine calling for HIS Servant. How could it be then that when the LORD was at the peak of calling Him, the world too was at the climax of heightening His career development and progression? By all worldly standards, in the manner of the description of the MAN OF GOD'S former career options, every average person would have loved to be found in that lofty place of flamboyance and significance. However, we can only come to one conclusion that many times when the LORD is busy calling somebody, then the world also often steps up its pressure of *elevating* them, and *directing* them in a totally *different,* and actually *antagonistic* direction. For those of us who are able to discern in the Spirit, this resistance by the world to release the MAN OF GOD was definitely the work of the adversary. Promotions or not, cancers or aerospace medicine, this must have

THE CIVIL AEROSPACE MEDICAL INSTITUTE (CAMI).

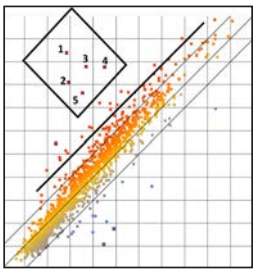
THE MAN OF GOD (CIRCLED) IN THE ANNUAL GROUP PHOTO SHOOT WITH OTHER PROFESSIONALS AND AUTHORITIES IN VARIOUS DISCIPLINES AT THE CIVIL AEROSPACE MEDICAL INSTITUTE (CAMI).



DNA Microarray Analysis Typhoon



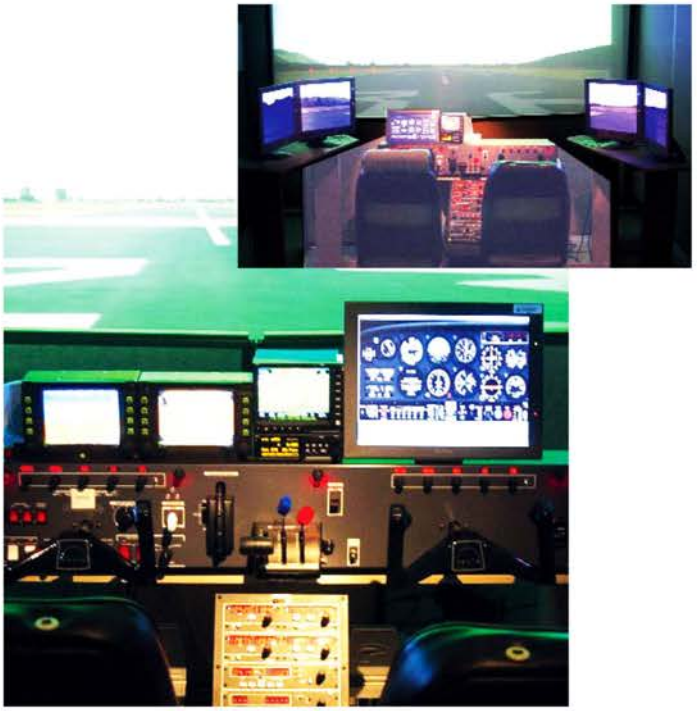
cDNA Microarray Fingerprint



Software Modelling of DNA Microarray Fingerprint

considering how much the LORD uses Him today. So was the case with the MAN OF GOD'S Calling. We can clearly see that the more the LORD became quite *relentless* in calling HIS Servant, the more His career *shot up* into the *skies*, and in this case, literally even in the real sense of the word *sky*. It is plainly *evident* that the overall intention of the world at that time, was to ensure that the Servant of the LORD would be totally *engaged* and fully *preoccupied* with serious matters of *research* and *science,* to the extent that He should not ever have time to accept the POWERFUL CALLING of the LORD that was awaiting. It was during the peak of His *colourful* career at the Cancer Institute of New Jersey (CINJ), that the MAN OF GOD again had to disrupt that *tenure track* for a more *lucrative* and *flamboyant dream* job offer. The only difference now being that this time around, He was invited to take up a very *senior position* as a *Consultant-Contractor* with the Federal Government. However, the MAN OF GOD had not known that the more He presented His research papers at the different Cancer Research Fora, the more the Federal Government was pursuing His skills. This went on across the different scientific gatherings from meetings on *Toxicology, Pharmacology, Signalling,* and *peptide* sciences. To prove that the world indeed did not want the MAN OF GOD to heed the CALLING OF GOD, things moved too fast for Him as the Federal Government right away paid for His flight ticket and put Him up in an expensive hotel in order that He may take up this

AGARS and BGARS - *continued from page 23*



Genes - *continued from page 3*

From left to right: Mark Huggins, Dr. Dennis V. Canfield, Dr. Nicole T. Vu, Dr. Hua Zhu, Dr. Edward D. Owuor

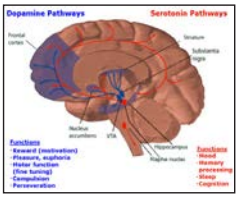
stand gene-level changes and the mechanisms that create adverse reactions in the body. Familiarity with such genetic-level reactions may allow scientists to develop biological mitigation techniques to prevent aircraft accidents and incidents.

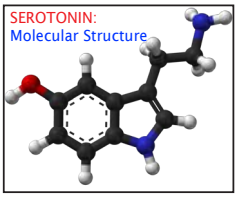
Researchers are examining how drugs, alcohol, radiation, fatigue, stress, and a broad range of other environmental factors, affect gene expression. Examining the varying gene expression patterns is significant in clarifying how the body reacts to certain stressors. By understanding that reaction, researchers can take the steps necessary to enhance proactively aviation safety and performance in flight crew and air traffic controllers.

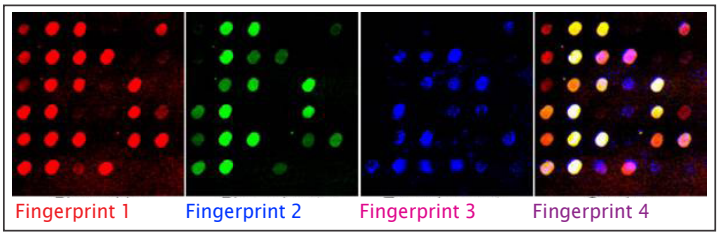
For example, among other projects, CAMI's functional genomics researchers are currently identifying target molecules of alcohol intoxication so they can develop strategies for prevention of performance impairment. They are also identifying the molecular networks that signal fatigue so they can identify the biomarkers of fatigue for accident investigation and prevention. This and other genetic groundbreaking research will help the FAA save countless future lives.

appointment. They then went ahead to secure for Him a huge home in a top neighbourhood called Covington Manor in Edmond. It teaches a very serious lesson that whenever the LORD CALLS one, they ought to be very cautious with what the world begins to throw at them! The world puts up a stiff resistance by throwing at them the huge mansions of this world, the gold, the diamond, and the silver! In talking with the MAN OF GOD, He never stops *lamenting* and *repenting* day after day, and saying that our mansions are not in Edmond, but in heaven where the glorious Kingdom of GOD is. The MAN OF GOD keeps emphasizing that He *erroneously* took up the position at the Civil Aerospace Medical Institute (CAMI), of the Federal Aviation Administration (FAA), within the Department of Transportation of the US Government. The taking up of that position amounted to defying GOD and attempting to running away from GOD's CALLING. Nonetheless, to be more specific, the MAN OF GOD THE PROPHET took up the assignment at the Department of *Forensic Toxicology and Aircraft Accidents* of the Civil Aerospace Medical Institute (CAMI). At that Department, the PROPHET OF THE LORD became part of a *high-calibre* team that was deeply involved in *death investigations*. The MAN OF GOD was charged with the responsibility of addressing *aircraft accidents, incidents*, and their *prevention* by learning from *aircraft crashes* and *fatalities*. This aircraft accident prevention program tasked Him with the novel job of developing a *DNA microarray fingerprinting and profiling platform* for examining gene expression fingerprints of pilots, before and after *aircraft accidents*. Nonetheless, this *DNA fingerprinting profiling* that the MAN OF GOD THE PROPHET developed, was not only limited to *Captains* and *First Officers* in charge of flight control, but also extended to embrace the entire *human element* in civil aviation. This encompassed *Flight Engineers, Flight Crew, Ground Traffic Control* and *Air Traffic Controllers*. At this place, the MAN OF GOD was firmly *riveted* with the responsibility of *examining* the human factors that affect the operation of an aircraft and especially in the *cockpit*, among *Civil Aviators* (Airmen, i.e. Airline pilots). He was charged with *detecting* human performance *impairment* in the cockpit of an aircraft, and especially how a *slower reaction time* by a Pilot can translate into the severe consequence of an *aircraft crash*.

This kind of *lofty* analysis of gene-specific DNA Microarray *fingerprinting* in *Forensic Pathology*, is what finally opens up a new front in the earlier *detection* of *alcohol abuse, drug abuse, clinical depression, irritability* and *violent behaviour* among airline Pilots. This kind of study is equally competent to catalogue the corresponding effects of such *insults* on the Pilot's ability to operate an aircraft. It is such analogue data that was then convertible into digital information for display on a normal desktop monitor. The interpretation of such *digital information* was then possible through a special Canadian software called *Array Vision* for *gene modelling*. This kind of DNA fingerprint gene modelling is what enabled the plotting of the gene behaviour in the said subject. DNA microarray *fingerprint* profiling that the PROPHET OF THE LORD brought into *Forensic Pathology & Aircraft Accident* Investigations, is what offers a brand new avenue for *piecing* together what could have happened in the *flight deck* before the crash. This analysis is what also enables *Crash Investigators* to rule out aircraft *mechanical factors,* and *human performance impairment*, thereby allowing investigators to focus on external factors like *lightening*, and *foul* play such as *terrorism*. This was the way in which it is possible to put in place AIRCRAFT ACCIDENT PREVENTION MECHANISMS & policies to reduce fatalities. This is because it is now possible to *detect* and *catch* the Pilot's clinical condition earlier as they report to the Office of Aerospace Medicine for their regular medical *exams,* and *recertification*. Any Aviator that is found *POSITIVE* for *drugs of abuse* or *alcohol abuse*, or under *depression,* is immediately *de-certified* as a *prevention* mechanism, to save life. That is how the MAN OF GOD'S work greatly impacted on Airline Pilots' Policy. The *veracity* of such work is that the *Standard Operating Procedure* should be *irrefutable* and be able to withstand a rigorous *legal* process in court.







Recertification with Distinction

FAA Laboratory Earns Prestigious Honor

The Forensic Urine Drug Testing program of the FAA's Civil Aerospace Medical Institute (CAMI) has earned recertification with distinction, for a second consecutive time, from the College of American Pathologists (CAP), of Northfield, IL. This is a rare honor, and it is one made even more special because it was awarded by a national organization of working peers.

This marks the second evaluation in a row in which the CAMI laboratory earned perfect scores in on-site inspections. No deficiencies were found during the on-site inspection or in the Lab's most recent prior inspection in 2001. Both inspections included a long and detailed review of hundreds of items, including the lab's staffing, physical plant, equipment, policies, and procedures, as well as the Lab's performance on testing materials received from the pathologists' organization during the last two years.

The CAMI laboratory has long served as the primary national toxicology testing site for federal agencies, including the FAA and the National Transportation Safety Board. Testing is routinely conducted on a wide variety of biological specimens, involving both living and deceased individuals. Dennis Canfield, Ph.D., is Manager.

"Both times it was noted by the inspectors that the CAMI lab is a 'Superior' laboratory," said John Soper, Ph.D., CAP scientific director for the CAMI laboratory. "Specifically, the inspectors said CAMI performs work far beyond the capabilities of most forensic urine drug testing labs, and should be considered as a national reference lab. We are extraordinarily pleased to earn this recertification with distinction, which is recognition of the hard work our staff has long been known for."

The pathologists' Forensic Urine Drug Testing Accreditation Program reviews Laboratories that perform urine drug testing for non-medical purposes (i.e., workplace drug testing). The lab must have specific staff, resources, and procedures in place, and undergo complete periodic on-site inspections.

"Urine drug testing is not only a condition for employment, but periodic testing can be conducted on people who work as pilots, members of flight crews, or air traffic controllers," Soper said. "When specimens are available from flight crew fatalities, CAMI also conducts after-death tests on various biological samples in addition to urine."

From left to right: Mark Huggins, Dr. Dennis V. Canfield, Dr. Nicole Vu, Dr. Hua Zhu, Dr. Edward Owuor

Urine drug testing is a critical component in the efforts to fight drug abuse in this country because it can objectively identify drug users in a variety of settings. Because of the legal consequences of a positive drug test, such tests are considered "forensic" testing. Therefore, it is crucial that laboratories maintain high standards of quality assurance/quality control.

The goal of the CAP Laboratory Accreditation Program is to improve the quality of forensic laboratory services through professional peer review, education, and compliance with established performance standards. Participation in CAP review is voluntary. Laboratories earning CAP accreditation mirror Federal standards and meet the highest standards of practice.

The Civil Aeromedical Institute is the medical certification, research, education, and occupational health wing of the FAA's Office of Aviation Medicine. CAMI's work focuses on the human element in flight - pilots, passengers, air traffic controllers - and the entire human support system that embraces civil aviation. ■

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Office of Aerospace Medicine
Washington, DC 20591

Isolation of RNA From Peripheral Blood Cells: A Validation Study for Molecular Diagnostics by Microarray and Kinetic RT-PCR Assays — Application in Aerospace Medicine

Nicole T. Vu
Hua Zhu
Edward D. Owuor
Mark E. Huggins
Vicky L. White
Arvind K. Chaturvedi
Dennis V. Canfield
James E. Whinnery

Civil Aerospace Medical Institute
Federal Aviation Administration
Oklahoma City, OK 73125

January 2004

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Office of Aerospace Medicine
Washington, DC 20591

Index to FAA Office of Aerospace Medicine Reports: 1961 Through 2012

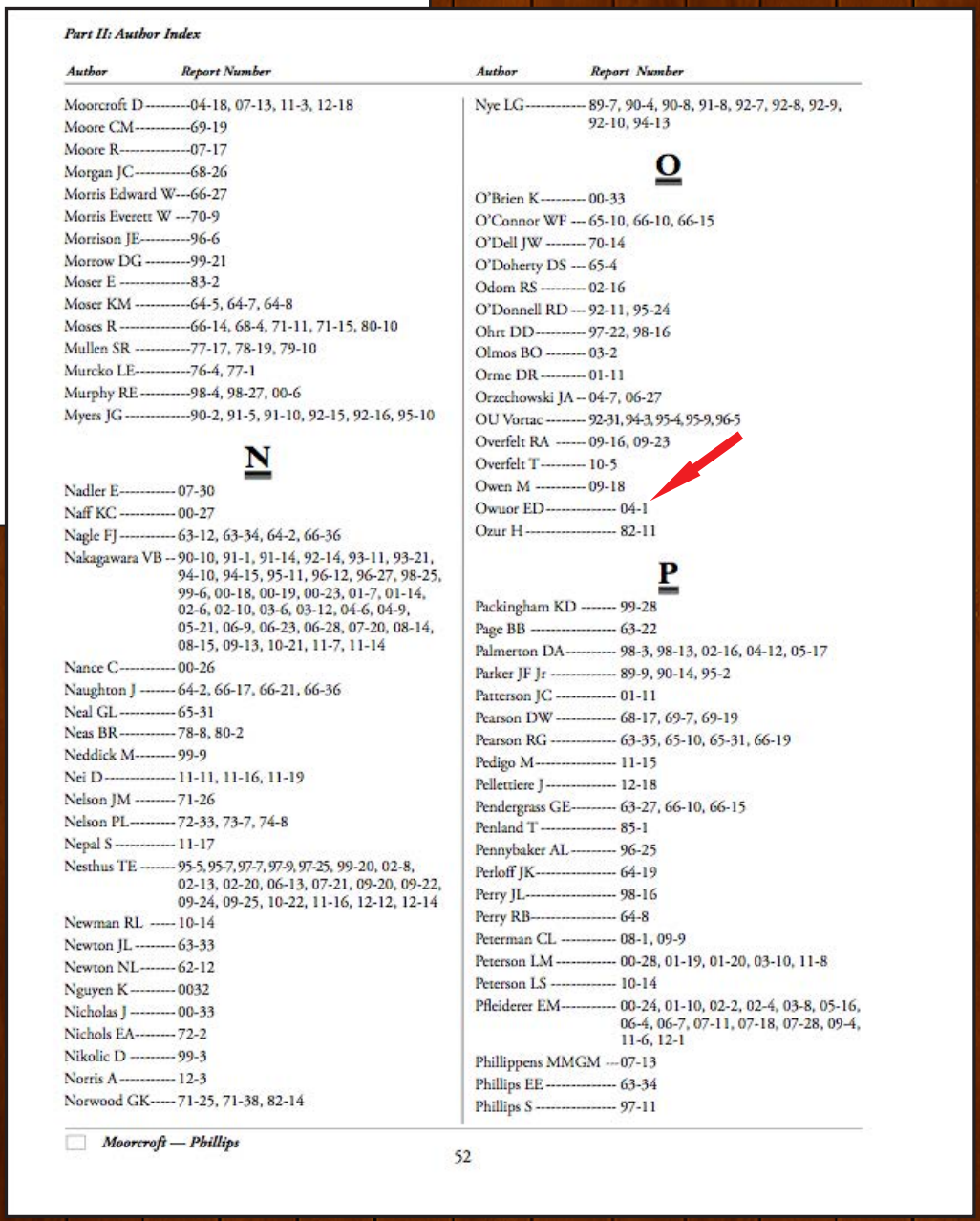
William E. Collins
CNI Aviation, LLC
Ada, OK 74820

Michael E. Wayda
Civil Aerospace Medical Institute
Federal Aviation Administration
Oklahoma City, OK 73125

January 2013

Final Report

IMPORTANT!



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While it is difficult to dispute this MIGHTY MAN OF GOD, however, since I had already set out to interrogate this revival and its Messenger, I had to do the necessary. After He had spoken with me in greater depth about His work in Aerospace Medicine, I set out to search for His stripes in that field and see if I could pull out anything. I must say that I was indeed very shocked, and puzzled to find out that in the updated FEDERAL AVIATION ADMINISTRATION (FAA) OFFICE OF AEROSPACE MEDICINE in WASHINGTON DC, their current 2013 INDEX OF AEROSPACE MEDICINE where Top Scientists who have ever made the most significant contribution in the field of Aerospace Medicine and Aircraft Safety, the MAN OF GOD'S name appeared under the INDEX 'O' on page 52 as 'Owuor ED'. This stunned me very much and made me understand very well that indeed when the LORD CALLS one, everything else is laid down in honour of the LORD OUR CREATOR. This was so big I had to publish it here as it is, that the world may know of GOD'S CHOICE. These are indeed the STRIPES the MIGHTY PROPHET OF THE LORD left in Academia with DISTINCTION.

GOD'S RELENTLESS PURSUIT

Washing Dirt From The House Of The LORD At A Very Tender Age

What is most *baffling* is that many times when the LORD calls somebody, the *footprints* of that calling can be traced way back in their early childhood. For instance, when Samuel the PROPHET OF THE LORD was called, it was at a very tender age. Jeremiah the Prophet also writes about the calling of one in the womb.

> Before I formed thee in the belly I knew thee; and before thou camest forth out of the womb I sanctified thee, and I ordained thee a prophet unto the nations (Jeremiah 1:5)

So was the case with the MAN OF GOD THE PROPHET when the LORD began to call him. JEHOVAH THE GOD OF ISRAEL had earlier marked the MAN OF GOD and caused him to work in the church at the tender age of 14yrs. It was during that work at the Altar of the LORD in the church, that some very *interesting* and indeed *intriguing* events took place, that today form the footprints of the LORD'S calling in his life. Apparently, the MAN OF GOD was at that tender age assigned the role of *cleaning* the church every Saturday in preparation for the Sunday Service. As time went by, eventually this work of cleaning the church became quite *cumbersome* and *tedious* because of the community within which that church was located. In that community, where the church was located, the few public toilets that were available, used to be washed and cleaned only from Monday to Friday. That created a serious *distress* as the toilets would fill up during the weekend and become totally unusable. It is because of this strain in public facility that some of the residents of that community unfortunately chose the church as the place to *relieve* themselves. That was made possible because the church doors remained opened throughout, and anybody could access the church anytime even in the deep of the night. Thus, when the MAN OF GOD at his tender age of 14yrs came to prepare the church on Saturday's for the Sunday Service, he would always find that the House of the LORD had been *soiled* with human excrement. It was a *despicable* sight to behold! That is when the MAN OF GOD would spend a lot of time *cleaning* up the mess from the church, and afterwards using water and soap to really scrape the floor and render the church ready for the Sunday Service. Unfortunately for him, whenever he cleaned on Saturday and got everything ready, upon coming early morning on Sunday, he could still find some fresh *soiling* that had happened on Saturday night. And that would hence send the MAN OF GOD into a very busy rush program of *re-cleaning* the church to ensure that by the time the worshippers begin to arrive, the church would be ready for GOD'S holy service. That is how it continued to be, that the MAN OF GOD would wash the church barefooted without even paying attention to the health hazard that would cause him. Remember that at that age he did not own any pair of sandals let alone shoes! After washing the church clean, the MAN OF GOD would rush to set up the LORD'S table by *dressing* it with a white table cloth that he had washed, and then put all the worship articles in place. The worship articles that the MAN OF GOD arranged included the flat *golden plate* for the LORD'S *offering*, and the bible stand on which the Reverend would place the bible as he read it, and the MAN OF GOD would set the bible in place. Then he would carry all the chairs from the church office and bring them into the main *Sanctuary* and arrange them accordingly. That is when he would sit down at one corner, alone, tired and dozing as he waited for the worshippers to start arriving. It was however on one Saturday, when the MAN OF GOD at his tender age had just finished *cleaning* up the church and brushing the floor very clean with soap, that he became very tired and went into the church office and sat next to the door. He did not turn on the office light where all things were kept, but just sat in the darkness with the door half open to take a small nap. As the MAN OF GOD sat

on that chair while dozing repeatedly nodding his head under the power of sleep and *exhaustion*, then he saw somebody walk in to the office. When he saw that *Somebody* had walked into the office, he woke up only to find that there was *nobody*. However, when the MAN OF GOD THE PROPHET tried to leave the office, then *Somebody* physically touched him so strong that he almost fell down. When he turned on the light to check who it was that had touched him, then he found that there was no one. That is when the LORD came in a subsequent day in a dream and told him "I HAVE TOUCHED YOU!" Of course, all these did not make for any *gravity* at that early age. But later when the MAN OF GOD was in High School and about to join university, he realized that there was something very *strange* about himself! To the extent that he was able to know so many months in advance when somebody was going to write him a letter and send it to him in school, and indeed when those months passed that particular letter arrived, that was strange! So was the case with many other occurrences around him. The MAN OF GOD could tell when certain things were about to happen and even *spookily* share with some of his colleagues, and those events would accurately take place. That was very *bizarre*! ONLY LATER when the LORD had called HIS Servant and sent him, is when the MAN OF GOD made sense of all that had happened to him in that old church when he used to *clean* the *soiling* of the church from the Altar of the LORD. Today he well understands that the LORD was doing with him as HE had done with other Servants such as Moses. When the LORD miraculously rescued Moses from the waters of the Nile, through Pharaoh's daughter, it was the prophecy of what the LORD was about to do with Moses in the future, that was being laid down (Exodus 2:1-11). The LORD was essentially saying that since even the name 'Moses' that he was given, meant, "I MIRACULOUSLY RESCUED HIM FROM THE WATERS OF THE NILE". So was the LORD too saying to Moses, that just as I miraculously *rescued* you from the deadly waters of the Nile, so will I use you in future to *rescue* my people Israel out of the *cruel* slavery from the land of the deadly Nile. That is how the *rescue* of Moses in his tender age, essentially forespoke the prophecy of GOD'S miraculous *rescue* of Israel from Egypt. And so was the case with the MAN OF GOD THE PROPHET. That when the LORD was using him in his tender age to *clean up* the *soiling* of the church by the enemies of GOD, so was HE foretelling the prophecy of how he would use the MAN OF GOD in these last days to *clean* up the *spiritual mess* that the enemies of GOD has brought into the house and used to *soil* up the holy place of *worship*.

THE LORD CALLS HIM FROM MOUNT CARMEL

During all these complex career undertakings, the LORD did not relent in *Calling* His Servant. Right from Israel, as he pursued his Doctoral thesis on Mt. Carmel at the University of Haifa, JEHOVAH repeatedly visited with HIS Servant in very mighty visitations. One such case was when the LORD Spoke with him in a mighty dream, in which the GOD of Israel came down to *Call him* for the first time. In that 1996 *inaugural Dream*, Heaven Opened, and the fearsome CLOUD OF GOD descended all the way from heaven and stood right before him. That is when the LORD Spoke to him by Voice from the CLOUD and *Called* His name twice, and he answered back. However, in that Dream, the LORD GOD ALMIGHTY also made it clear to him that when he accepts the *Calling* to serve CHRIST Jesus the Messiah, he would have to *forego* all his future *academic aspirations* that he had held so dear to his heart. Out of the *fear* of the unknown into which the LORD was seemingly throwing him, the MAN OF GOD THE PROPHET began to literally *run away* and flee from the LORD! The exact moment of reckoning nonetheless did not come until while in Israel, many of His colleagues at the University began to *shun* him. As all these happened, he did not understand that it was the LORD who had *orchestrated* all these alienation around him. The peak of that *alienation* came when one day he was walking into the Institute at which he conducted experiments for the Doctoral thesis, and he was stunned to observe that all the staff had *gathered* towards the end of the hallway, and were looking at him from afar as though he was very *strange*! In as much as that may have puzzled him, the MAN OF GOD did not seem to be moved since he simply continued on with his work. It was not until one day when as he again entered the Institute gate, and once more his entry saw everybody gather in the hallway, peeping at him through the glass door. That is when he was finally prompted to ask some of his colleagues this question, "*Haven't you ever seen a black person*?" And in response, one of the Professors answered him back by saying, *"Do you remember Moses? How could he lead us all the way from Egypt and bring us here?"* Baffled by that response, the MAN OF GOD THE PROPHET did not seem to understand what that answer was upto. Then the MAN OF GOD went on with his work and ignored that episode.

THE CITY OF CHICAGO

However, when the MAN OF GOD had finally moved to the US and settled in Chicago, He then began to work at the Chicago Medical District which essentially encompasses the Rush Presbyterian Hospital, the notorious Cook County Hospital, and the UIC Medical Center. It was then that one day as He was walking towards the Chicago EL, on Washington Boulevard in Forest Park, Illinois, someone that was driving in the opposite direction, hooted at him and pulled over in the next driveway. When that person called upon the MAN OF GOD to attend to him, the MAN OF GOD was indeed very shocked at the *utterances* of this man. The man who appeared to be in his upper 50s, still seated in his car, stretched out his hands to greet the MAN OF GOD. But as the MAN OF GOD extended his hands to that man, he began to say, *"Sir, I don't know whether you know this, but as you were walking, I saw so much bright light cover you and it was so blinding that I almost ran into an accident."* *"Sir,"* that man added, *"Do you remember Moses?"* And then, even before the MAN OF GOD could respond to him, he kept reaching out at the MAN OF GOD'S hands that greeted him while saying, "*Look even your hands, these are healing hands. They are so warm. These are healing hands!*" The MAN OF GOD looked at him in shock and answered him, "*Sir, it must be the Jesus I received that you are seeing.*" That is when the MAN OF GOD quickly abandoned that conversation and walked away towards Roosevelt Avenue and into the Medical District of Chicago where he worked. That was the first time the MAN OF GOD THE PROPHET finally connected the "*Do you remember Moses?*" that the Israeli Professor had advanced towards him on Mt. Carmel, and this, "*Do you remember Moses?*" of Chicago. His fears finally came true when he began to realize that the LORD GOD had eventually *cornered* him and *caught up* with him.


Chicago

THE LORD APPEARS TO HIM

While still in Chicago, one day the LORD appeared to the MAN OF GOD in his Forest Park apartment in a stunning Dream. On that night, the MAN OF GOD THE PROPHET knelt down right next to his bed and prayed. But in that prayer, the MAN OF GOD literally spoke to the LORD using the following words, "LORD, was that you in the bright light that these people are seeing around me and asking whether I can remember Moses?" In that direct conversation with the LORD, the MAN OF GOD further went on to ask the LORD to confirm to him, whether it was HE THE LORD that had brought that *light* to bare around HIS Servant; the *Light* that made people in Israel and Chicago, to ask the question, "Do you remember Moses?". As though to answer the MAN OF GOD directly, that very night the LORD appeared to him in a tremendous Dream, standing right between the entrance and the Kitchen area of his house. In that visitation, the *radiant* CLOUD OF GOD'S Glory was hoovering around where the LORD was standing in an episode that shocked the MAN OF GOD and caused him to jump up from the Dream. He then went on his knees and *repented*, telling the LORD that he did not mean it, when he asked for a *sign of proof*. After that, some silence ensued as the LORD did not visit again for sometime.

THE LORD breaks his collar-bone

When the MAN OF GOD took up the appointments at the College of Pharmacy & at the Cancer Institute of New Jersey, the LORD followed him there. In one visitation, the LORD Spoke to him about *resigning* from his job and stepping out to preach the glorious gospel of the COMING OF THE MESSIAH. However, as the MAN OF GOD continued to run away from the LORD and *disobey* the *calling*, the LORD on one occasion showed him a Dream in which HE THE LORD warned HIS Servant that if he continued to disobey and run away from THE LORD, HE would *strike him* with an accident. And in that Dream, the LORD presented to him the accident that was about to happen to him. A few days later, as the MAN OF GOD drove from Manahawkin towards New Brunswick where the Cancer Institute of New Jersey was, on the Garden State Parkway, all of a sudden, the accident he saw in the Dream took place. And his car rolled several times on a flat terrain that had no reason whatsoever to see that type of accident. As he was driving, the MAN OF GOD just realized all of a sudden that he had woken up in the Jersey Shore Medical Centre Emergency room. Later on that day, the Emergency Room Doctors came to the MAN OF GOD and told him what had happened to him. That he had rolled over in his car and the vehicle was mangled and totally written off. The Doctors then explained to him that at the accident site a piece of metal had hit his shoulder and his *collar bone* was broken. They went on to explain that he had to be cut out of the mangled car, with severe injuries suspected in the brain because blood was oozing out of his eyes. They then concluded by telling him that because of the *severity* of the accident, he had to be airlifted from the accident site to the Jersey Shore Medical Centre. From that point on, the Doctors passed the MAN OF GOD through a *memory test* and they asked him whether he could remember what *Project* he was working on at the Cancer Institute. The MAN OF GOD then responded on giving an *extensive discussion* on *Caspase-3 Cell Death Protease* that he was working on in drug discovery. And they all agreed that indeed, despite *profusely* bleeding through the eyes, his memory was purely intact. However, when they left him to stay overnight at the Medical Centre for observation, that is when he fell asleep and the LORD appeared to him in a Dream Saying, "YOU CANNOT RUN AWAY FROM ME". That is when the MAN OF GOD remembered that the LORD had warned about this earlier in light of the continuing *disobedience*.

THE LORD SHOWS HIM THE CROSS

It is as though JEHOVAH THE GOD OF ISRAEL was simply awaiting the *fullness* of time in order to move in and command HIS Servant to follow HIM. And then when the *fullness* of time came to pass, the LORD stepped up HIS *relentless* visitations unto the MAN OF GOD, by increasing the frequency of *dreams, vision, visitations* and by *Speaking* to HIM by *Audible Voice*, as a MAN Speaks with a Friend! All those conversations were geared at the need for the MAN OF GOD to finally give up and step out and serve JESUS the Messiah. Throughout all His Career from Israel into the Civil Aerospace Medical Institute, the LORD GOD ALMIGHTY was *ceaselessly* in

SHOCK & STUN AS GOD BEAMS HIS GLORY ALL THE WAY FROM HEAVEN ONTO HIS PROPHET

Kakamega, Sept 1-2, 2012 Heaven Beamed on Him & Pointed the nations to HIM.

Kakamega, Sept 1-2, 2012 And Heaven Pointed the nations to HIM.

Nakuru, August 11, 2013 Heaven Beamed on HIM.

Nakuru, August 11, 2013 The Glory Surrounded HIM.

Nakuru, August 11, 2013 And the Glory Covered The MAN OF GOD'S Back Like Cotton Wool!

Nakuru, August 11, 2013 And the Glory Covered The Man Of GOD's Back Like Cotton Wool! See how the Glory from The PROPHET touched on the Cameraman's black trouser.

During the time the MAN OF GOD was doing His Doctoral Thesis on Mt. Carmel in Israel, many times the Professors at the Institute could all gather at the end of the hallway and look at Him in a strange and fearful way. But when He attempted to ask them why they were looking at Him in such a strange way, one of them once answered Him back by saying, "REMEMBER MOSES! MAKE SURE YOU REMEMBER MOSES THE PROPHET!" This kind of situation bothered the MAN OF GOD for a very long time because He did not understand what all this was about. However, when He graduated with a Doctorate from the University of Haifa, and moved to work in the US, again the same situation recurred to Him. One time when He was walking to the UIC Medical Centre where He worked in Chicago, as He walked on Washington Blvd, which was a one way traffic road that connected Roosevelt Avenue to Forest Park Illinois where He lived, then a man driving a car began to hoot aloud at Him. When the MAN OF GOD who was walking in the opposite direction on Washington Blvd, turned in the direction of that car, the car pulled over into one of the driveways, and the driver called on the MAN OF GOD. When the MAN OF GOD went to attend to that man supposing that he was looking for direction to a place, then that man began to say, "SIR, I DON'T KNOW WHETHER YOU KNOW THIS, BUT WHILE YOU WERE WALKING ALONG THIS BOULEVARD, I SAW TREMENDOUS BRIGHT LIGHT COVER YOU TO THE EXTENT THAT IT ALMOST BLINDED ME, AND I ALMOST SWERVED INTO THE DRAINAGE BY THIS GAS STATION." As the MAN OF GOD was still in shock at those sayings, that man went on to add, "SIR, DO YOU REMEMBER MOSES?" As that man greeted the MAN OF GOD, he added, "AND THESE ARE WARM HANDS! THESE ARE HEALING HANDS!" Unaware of what this stranger was talking about, the MAN OF GOD decided to walk away as He told that stranger, "SIR, I THINK IT IS THE JESUS I RECEIVED THAT YOU ARE SEEING AROUND ME." However, as the MAN OF GOD walked away, that was the first time He was able to connect the, "REMEMBER MOSES" of the Professors in Israel, and this, "DO YOU REMEMBER MOSES" of Forest Park, Illinois. This greatly troubled the MAN OF GOD especially that He was trying to flee from THE LORD'S CALLING. However, when the MAN OF GOD began working at the Department of Forensic Toxicology & Aircraft Accident at the Civil Aerospace Medical Institute, once again His colleagues began to do the same thing He had gone through in Israel. They would all gather at the end of the hallway whenever the MAN OF GOD walked towards His office, and they would look at Him very strangely in a manner that again bothered Him. That is when one of His colleagues one time, took the courage and towards the MAN OF GOD as He entered the hallway, and met Him right before He entered His office, and said the following words as He shook the MAN OF GOD'S hand, "DOCTOR, I CAN SEE THAT EVEN YOUR HANDS ARE ACTUALLY WARM! THESE ARE HEALING HANDS." However, one other Doctor from Forensic Pathology stepped in and said, "MOSES, HOW ARE YOU DOING?" This shocked the MAN OF GOD a great deal. And to make matters worse, one time when He took His car for servicing at the Chrysler Service Bay, after finishing the paperwork in the Manager's office and was leaving, as the Manager of that service station walked Him towards the door, he made the following comment to the MAN OF GOD, "SIR, WHEN I LOOK AT YOU I REMEMBER MOSES OF THE BIBLE." Now coming from a Manager at the Chrysler Service Bay, this is what greatly shocked the MAN OF GOD and shook Him to the core, to the extent that the paperwork He had in His left hand dropped to the ground! And deep down in His heart the MAN OF GOD knew that finally GOD had not only caught up with Him ,but also cornered Him that He may go serve HIM. However, today we see that in the September 1, 2012 Kakamega Grand Revival Meeting, and August 9-11, 2013 Mega Nakuru Revival Meeting, THE LORD BEAMED THE WHITE GLORIOUS COLUMN OF HIS GLORY FROM HEAVEN ONTO HIS SERVANT, TO THE EXTENT THAT PEOPLE WERE ABLE TO RECORD ON CAMERA, THAT SHOCKING GLORY MOVING AROUND WITH THE MAN OF GOD FROM PLACE TO PLACE. Now we can indeed understand what the Israelis and the Americans were seeing around the MIGHTY PROPHET OF THE LORD. GOD MOST HIGH HAD MARKED HIM, AND WAS POINTING THE NATIONS TO HIM AS HE THAT PREPARES THEM (John 1:33)!

NAKURU, KENYA / August 11, 2013

And The LORD GOD Literally Transfigured HIS PROPHET In The Healing Service. And The Glory Covered His Back Like Cotton Wool!

hot pursuit to *call* HIS Prophet, while the PROPHET OF THE LORD on His part was always making serious attempts to flee from the *Calling* of JEHOVAH. And then it came to pass that just as Israel went out of Egypt, so did the *selfsame* day come to pass for the MAN OF GOD to leave this *milieu* of complex career track in response to serving the LORD GOD.

> 41 And it came to pass at the end of the four hundred and thirty years, even the selfsame day it came to pass, that all the hosts of the LORD went out from the land of Egypt (Ex 12:41).

It however did not come as a joke, but it came with one major vision in which GOD THE FATHER showed the MAN OF GOD the horrendous *agony* and the *pain* of how the LORD JESUS was *crucified* on the Calvary Cross. HE SHOWED HIM THE PASSION OF THE CHRIST. This caused him to *weep* for three straight months and *rendered* him totally *dysfunctional*. The LORD showed HIS Servant Christ JESUS on the Cross, tossing and turning at the pain of the moment. In that vision, GOD Showed him how Christ was crucified, the agony and pain and how HE went down under. Then the LORD took him under to see how the leopard wanted to attack the Christ on the Cross but POWER came from on high and struck the underground. And there was an earthquake after which a tremendous Blinding Glory that struck the underground eventually lifted the Messiah like lightening as he went in TRIUMPH! That is what dealt the *final blow* that ultimately crushed Him to give up his *lucrative* career tenure track and faithfully follow the LORD with all his heart from that day todate. It is a shock that shook him and sent him preaching the gospel of THE COMING OF THE MESSIAH, world over, to this day. AFTER THE PROPHET OF THE LORD gave in to the Calling of GOD, and stepped out of the world of science, the LORD then found a friend that he could confide in and hence visited him in a monumental fashion. In that visitation, the LORD finally appeared to HIM in a tremendous visitation that can only mirror biblical proportion. The CLOUD OF GOD appeared to him and further *disarmed* him from ever pursuing anything earthly occupation. In that historic vision,when the CLOUD descended from heaven, GOD Spoke with HIM by *Audible Voice* on the MISSION that was at hand.

THE CLOUD SPEAKS WITH HIM FROM THE ARK OF THE COVENANT

In one of those visions at the onset of HIS *calling*, GOD ALMIGHTY lifted HIS PROPHET in the Spirit from the earth and took Him into the Throneroom in Heaven, and presented the ARK OF THE NEW COVENANT OF GOD right before Him. In that astonishing visitation, the CLOUD OF GOD then came through the *golden walkway* that marks the Throneroom in Heaven, and SAT on the Mercy Seat of the ARK OF THE NEW COVENANT. At that moment, the MAN OF GOD THE PROPHET was then able to see Moses the MAN OF GOD seated next to the Mercy Seat of the Ark of GOD, and Elijah the Prophet of the LORD seated right next on the same side of the Mercy Seat of the Ark of GOD, and Daniel seating alone next on the other side of the Mercy Seat of the Ark of the Covenant. With Moses and Elijah on one side, and Daniel on the other, it was then that GOD ALMIGHTY Spoke to HIS Prophet by Voice from the CLOUD that sat on the Mercy Seat of the Ark of the Covenant and Said these words, "TODAY I HAVE MY FOUR PROPHETS HERE, AND YOU ARE THE FOURTH PROPHET, AND POWER HAS TODAY BEEN GIVEN TO YOU." At that juncture, the MAN OF GOD'S bed literally *shook* like an earthquake had hit HIS house. Upon waking up in shock and scream, the MAN OF GOD looked at the clock that sat on the bedside table, and realized that it was exactly 3:26am. It was then that He immediately

MOI UNIVERSITY IN ELDORET THROWN INTO GREAT SHOCK AS THE LORD OPENS THE EYES OF A TOTALLY BLIND STUDENT

Sonia Oduor became totally blind 10 years ago after a chronic illness. She was only able to get her way around by the help of the White Cane. She was totally blind to the extent that she only studied using Braille. And getting around the University sometimes became a great challenge, because one time she fell in a septic hole and broke her leg after missing to spot it. BUT COME THE JUST ENDED MEGA ELDORET REVIVAL MEETING, ON APRIL 19th, 2014, just as the MAN OF GOD THE MIGHTY PROPHET was leaving the grounds, the LORD popped open her totally blind eyes in a very dramatic and shocking manner that made everyone go wild in a total celebration. Here we see the University Students celebrate in a very Historic way as they walked around with her throughout the field, throughout the town and all over the University, till it caught the attention of the University Administration. In the picture above, we can see that she is able to identify the handkerchief that was extended to her and she reached out for it, and took it. The University Administration hence wrote a letter of appreciation to the MIGHTY PROPHET OF THE LORD. GLORY TO JESUS! GLORY TO GOD MOST HIGH! These are the days that we live in, the Days of HIS GLORY, THE DAYS OF HIS PROPHET!

MOI UNIVERSITY
OFFICE OF THE DEPUTY VICE CHANCELLOR
STUDENTS AFFAIRS

Tel: (053) 43620
Fax: (053) 43047
Email: dvcsa@mu.ac.ke

P.O. Box 3900
Eldoret - 30100
Kenya

Ref: No. .....

16th May, 2014

Prophet Dr. David Edward Owuor
The Mightiest Prophet of the Lord
Ministry of Repentance and Holiness
P.O. Box NAIROBI

Dear Prophet Dr. Owuor

RE: THANKS GIVING

I would like to thank you very much for the national thanks giving and healing meeting that you held at Eldoret Sports Club in April 2014.

Many of our students attended the meeting and the following two reported to have gotten healing from their previous conditions:

1. Sonia Oduor according to our student' records joined the University with blindness. She attended your meeting and her eyes were opened and now she can partially see and recognise colours.
2. Janet Jelimo has been suffering from diabetes with high blood sugar. After attending your meeting, she presented me a test from our University clinic indicating that her sugar level is normal.

I would like to thank your Ministry for what the Lord has done in the lives of our students.

Yours sincerely,

Prof. Nathan Oyori Ogechi
DVC, Student Affairs

(ISO 9001: 2008 Certified Institution)

MOI UNIVERSITY STUDENTS ORGANISATION
MUSO IN UNITY WE STAND

M.U.S.O.
MOI UNIVERSITY
P.O.BOX 3900
ELDORET

DATE: 16TH MAY, 2014

FROM: MOI UNIVERSITY STUDENTS ORGANIZATION

TO: THE MIGHTIEST PROPHET OF THE LORD,
DR. DAVID EDWARD OWUOR

RE: THANKSGIVING

On behalf of Moi University Students' fraternity, I wish to convey our unquantified gratitude to God and his servant, the Mighty prophet. Hope came to Eldoret, it gave our students a reason to live again, indeed it was a story of "he touched me and I saw a difference."

The national healing and thanksgiving meeting held on 18th to 20th April, 2014 remains the most important and significant meeting attended by our students. Two students whose details follow were healed, the records were availed and every doubting Thomas was convinced that God's hand passed and left a physical mark for the world to see.

1. **ODUOR AMONDI SONIA REG. NO: EDN/64/13 Was blind, today she sees**
2. **CHELIMO JANET REG. NO: EDS/1042/12 Was diabetic, today she is free**

Though an institution of higher learning that appeals to science as its founding stone, it has remained indelibly clear and resolute in its emphasis that its only through the consent of God and the act of his chosen messenger the Mighty Prophet that science bows in humiliation and defeat.

God, thank you for sending your servant, the Mighty prophet.

Prepared and duly signed by,

GEORGE BUSH

THE PRIME DIRECTOR, MUSO

KAKAMEGA MEGA REVIVAL / January 1, 2014

This young boy was totally Blind after a chronic eye disease, and immediately after the PROPHET OF THE LORD walked into the stadium, the LORD opened his Blind eye and HE did a mighty miracle of creation and, in the eyes of millions present, HE formed a new iris. Now he could see very well and even reached out for the bottle of Soda extended to him by the MAN OF GOD THE PROPHET

began to know everything that was going to happen in future, on the earth. That is when He understood what the statement, ' ..AND POWER HAS BEEN GIVEN TO YOU" meant. After a few days, the LORD again visited with HIS Prophet in a very mighty way in which He appeared in His House in a mighty vision, and stood at the door to the master bedroom. It was at that place that the MAN OF GOD saw the CLOUD OF GOD hoovering around the door and causing Him to shout, 'LORD, IF THAT IS YOU, PLEASE TAKE ME WITH YOU." Immediately, He finished uttering these words, The MAN OF GOD was terribly shocked in that vision to realize that He had been lifted up above the bed. However, the events that followed that lifting up, have still remained inaccessible to Him todate. The only thing that the MAN OF GOD remembers, is that He woke up in the third bedroom, from where He walked down the hallway to the master bedroom at which He had been lifted up.

THE WRITING ON THE WALL

Nevertheless, it was while back to the master bedroom of his house, that the MAN OF GOD was *slayed* by the LORD again and went into sleep, and saw the vision in which the HAND OF GOD placed a plexiplastic kind of board on the wall above, and wrote in white the scripture, ISAIAH 43:11, 1. In that shocking vision, the HAND OF THE LORD took another transparent Plexiplastic of the same size and used it to cover the writing on the wall, as in protecting HIS WORD and *bolted* it with a white seal in a process that was deliberately geared towards jealously protecting and sealing and HIS WORD. The second part of that vision, became the part when the MAN OF GOD was lifted up by GOD HIMSELF and taken into Israel, and HE saw the place from which JOHN THE BAPTIST was Called and began his Ministry. It also included the drawings on the wall that his disciples engraved which portrayed his beheaded head on the wall, and that of his *Prophetic Finger*. In the third part of this mega vision, the MAN OF GOD then saw Himself preaching to millions and millions of people all across the earth and shouting, "REPENT AND PREPARE THE WAY, THE MESSIAH IS COMING, RETURN TO HOLINESS, PREPARE THE WAY OF THE LORD." That is when the MAN OF GOD woke up and went into the bible and read the scriptures that the LORD had written unto Him:

> "I, even I, am the Lord, and apart from me there is no Saviour." (Isaiah 43:11)

When HE read the next one then He understood that this was the Calling of the LORD as it said;

> "But now, this is what the LORD says— he who created you, O Jacob, he who formed you, O Israel: "Fear not, for I have redeemed you; I have summoned you by name; you are mine." (Isaiah 43:1) ■

ELDORET MEGA REVIVAL / APRIL 2014

The LORD removed this young man from the world of the silent immediately the MAN OF GOD THE PROPHET stepped foot on the Eldoret Sport's grounds, and now he was able to clearly identify sounds.