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EDITORIAL

Stimulating Expansion and International Recognition: Translational Medicine

1. Introduction

Translational medicine (*TM*) is gaining strength in medical practice and interventional epidemiology; it is a natural 21st century outgrowth from evidence-based medicine. TM integrates evidence of research from the basic, social, and political sciences. This affects maximally patient care outcome and prevention. TM can convert biological discoveries into practical applications of drugs and medical devices with the aim of optimal patient care. TM plays a key role in promoting "from bench to bedside" or from laboratory experiments through clinical trials to actual applications to patients. TM is, therefore, crucial in stimulating advances in applied science. For greater clarity of function, there is a move on to adopt a newer, perhaps, more appropriate term: translational medical science. Because, in the best sense, medicine is not a science, it is a clinical practice of healing patients, whereas science addresses principles and experimentation enhanced by the addition of indispensable tools, for example, statistical analysis. Let us examine briefly a few pertinent examples. From these, we hope to focus the reader's attention on significant work being performed at Taipei Medical University.

Ho et al[1] evaluated the pathophysiological effects and possible mechanism of nitric oxide (NO) on osteoblasts; they used neonatal rat calvarial osteoblasts as the experimental model. Exposure of osteoblasts to sodium nitroprusside significantly increased caspase-3 activity. NO, decomposed from sodium nitroprusside, can induce osteoblast apoptosis through a mitochondrion-dependent cascade that causes mitochondrial dysfunction, release of intracellular reactive oxygen species and cytochrome c from mitochondria to cytoplasm, and activation of caspase-3.

Chen et al[7] evaluated the mechanism of NO-induced osteoblast apoptosis from the viewpoints of mitochondrial functions, intracellular oxidative stress, and anti-apoptotic Bcl-2 protein; they used neonatal rat calvarial osteoblasts as an experimental model. Administration of sodium nitroprusside (SNP) to osteoblasts led to DNA fragmentation when done time dependently. The mitochondrial membrane potential was significantly reduced after SNP administration, but SNP decreased Complex I NADH dehydrogenase activity in a time-dependent manner.

As another approach, Fu et al[2] tested the herbal extract 2,3,5,6-tetramethylpyrazine (TMP) for possible therapeutic efficacy against a glioma cell line and against gliomas transplanted into rat brains. In cultured glioma cells, TMP can suppress glioma activity, including growth. It can also protect neurons against glioma-induced excitotoxicity, suggesting that TMP may have therapeutic potential in treating malignant gliomas.

Large U.S. epidemiological cohort studies indicated that active and passive smoking are associated with increased breast cancer risk. However, there seems to have been no direct evidence that tobacco carcinogens can affect cellular molecules involved in breast tumorigenesis. Lee et al[3] used MCF-10A that are normal human breast epithelial cells in which the a9-nAChR subunit could be conditionally overexpressed by removing doxycycline from the culture fluid. Cell proliferation and soft agar assays and tumor growth in nude mice served as indicators of cell transformation. Results revealed that, in 186 (67.3%) of the 276 paired samples, a9-nAChR mRNA was expressed at (mean, 7.84-fold) higher levels in breast cancers than in surrounding normal tissues. Thus a9-nAChR plays an important role in nicotine-induced transformation of normal human breast epithelial cells.

Resveratrol (3,5,4' trihydroxy-trans-stilbene) is a stilbenoid, a type of polyphenol, and a phytoalexin is produced naturally by several plants when under attack by pathogens, such as bacterial and fungi. Juan et al[4] examined resveratrol's heme oxygenase-1 (HO-1) inducing potency and its induction of regulation in human aortic smooth muscle cells. They found that resveratrol-mediated HO-1 induction occurred in concentration- and time-dependent manners. However, this happened at low concentrations (1–10μM), and it was modulated at both the transcription and translation levels. Resveratrol-mediated HO-1 expression occurs, at least in part, through the NF-κβ (nuclear factor kappa-light-chain-enhancer of activated B cells) pathway, which might contribute to resveratrol's vascular-protective effect at physiological concentrations after moderate red wine consumption.

Experiments have investigated potential applications of 5,5-diphenyl-2-thiohydantoin-N10 (DPTH-N10) in treating human colon cancer. Subcultured human colon cancer cell line, COLO-205, served to examine antiproliferative effects of DPTH-N10 on colon cancer. Immunoprecipitation revealed that the formation of cyclin-dependent kinase 2–p21 complex increased in DPTH-N10-treated COLO-205. Kinase assay also revealed that cyclin-dependent kinase 2 activity decreased in DPTH-N10-treated COLO-205. DPTH-N10 caused inhibition of growth in COLO-205 by inhibiting DNA synthesis and by activating apoptosis, as reported by Lee et al.[5]

Ketamine is a drug used in human and veterinary medicine. It was originally created for use as a human anesthetic. Wu et al[6] evaluated ketamine: on regulating tumor necrosis factor-alpha (TNF-α); interleukin-6 (IL-6) gene expression; its putative signal-transducing mechanisms in lipopolysaccharide (LPS)-activated macrophages. Treatment with ketamine, concentration and time dependently, alleviated enhanced effects. LPS induced TNF-α and IL-6 mRNA syntheses. Results revealed that a clinically relevant concentration of ketamine could inhibit TNF-α and IL-6 gene expression in LPS-activated macrophages. Any suppressive mechanism occurs through

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suppression of TLR4-mediated sequential activations of c-Jun *N*-terminal kinase and activator protein-1.

Ketamine, as an intravenous anesthetic agent, can modulate vascular tone. NO is produced constitutively in endothelial cells and, therefore, contributes to vasoregulation. Chen et al[7] evaluated the effects of ketamine on NO biosynthesis and possible mechanisms in human umbilical vein endothelial cells. A clinically relevant concentration of ketamine can reduce NO biosynthesis; however, suppressive mechanisms occur by pretranslational inhibition of eNOS expression and by a posttranslational decrease in endothelial NO synthase activity; presumably, this is because of a reduction in intracellular calcium levels.

Propofol is used to induce or maintain anesthesia during certain surgeries, tests, or procedures. Chen et al[8] evaluated the anti-inflammatory and antioxidative effects of propofol on the biosyntheses of TNF-α, IL-1β, IL-6, and NO in LPS-activated macrophages. Exposure of macrophages to propofol significantly inhibited LPS-induced NO biosynthesis. Propofol, at a therapeutic concentration, exerts anti-inflammatory and antioxidative effects on the biosyntheses of TNF-α, IL-1β, IL-6, and NO, in LPS-activated macrophages. Suppressive effects at the pretranslational level were also revealed. Exposure to LPS and IFN-γ significantly increased endogenous nitrite production. In parallel with increased endogenous NO, administration of LPS and IFN-γ suppressed cell viability, mitochondrial membrane potential, and ATP synthesis. NO released from SNP induces osteoblast insults leading to apoptosis; the mechanism may involve modulation of mitochondrial functions, intracellular reactive oxygen species, and Bcl-2 protein.[9]

Chow et al[10] examined the protective mechanisms of quercetin (QE) on oxidative stress-induced cytotoxic effect in RAW264.7 macrophages. Activation of apoptotic proteins, including caspase-3, caspase-9, PARP, D4-GDI proteins was identified in H(2)O(2)-treated cells by Western blotting and by enzyme activity assay; they were significantly blocked by adding quercetin (QE), but not glycoside rutin (RUT) and quercitrin (QI). Induction of HO-1 protein may play a role in the protective mechanisms of QE on oxidative stress (H(2)O(2))-induced apoptosis and in the reduction of intracellular ROS production and mitochondria dysfunction by blocking apoptotic events. Differential anti-apoptotic effect between QE and its glycosides RUT and QI by distinct HO-1 protein induction was also defined. There are similar analyses aimed at clarifying apoptosis (Lugli et al[11]), glutathione (Ferraresi et al[12]), and mitochondrial membrane activity (Lugli et al[13]).

2. Perspectives

We have witnessed examples of translational medical science and how it may be translated to patient treatment. Clearly, its origins are rooted in TM. Translational research is another term for translative research and *translational science*. Translational research is a way of thinking about and conducting scientific research so that results are applicable to a particular population; it is practiced in the natural, biological, behavioral, and social sciences. In medicine, it is useful to translate results from basic research more quickly and efficiently into medical practice. Done successfully, the results yield meaningful health outcomes that can be physical, mental, or social. By removing barriers to multidisciplinary collaboration, translational research is now poised to push the advancement of applied science. In short, we might say "from bench to bedside" or from laboratory experiments through clinical trials to actual point-of-care patient applications.

Little did we know that this opening subject of *JECM* would be the last in formal association with our Founding Editor in Chief, President of Taipei Medical University, Wen Ta-Chiu; we will sorely miss him from this pivotal capacity as he moves on to newer challenges. We are appreciative, however, that he promises to remain nearby in the Ministry of Health. We are also gratified that he acknowledges what we are trying to do: bolster the excellence of *JECM*'s current trajectory. President Chiu has also pledged assistance as we implement an emerging initiative, that is, expansion for recognition by focusing on various "hot topics." There is an active recruitment of key persons to accept the challenge of Guest Editor with the hope that we may produce up-to-date review articles in special issues devoted to topics, such as Alzheimer's disease, public health policy, and TM. This new strategy is viewed as one that promises to catapult *JECM* more rapidly into an already saturated publishing milieu. *JECM*, amidst all this, must indeed establish a unique identity, truly international, not regional, and become a vital force in advancing biomedical research.

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