Could you start by introducing MAX BioPharma and its core objectives?

MAX BioPharma is a biotechnology startup company that was formed in 2010 around a platform technology of small molecule oxysterols. These molecules had been discovered in the laboratories of Dr Michael E Jung and myself at the University of California, Los Angeles (UCLA) and of Dr William Matsui at the Johns Hopkins Institute, and exclusively licensed from these great institutions. The core objective of the company is to develop lead candidates from this novel class of small molecules into next-generation therapies for a number of debilitating and fatal human disorders.

Our primary focus has been to find a new anabolic therapy for osteoporosis and bone healing that acts by stimulating new bone formation to replace the bone lost during ageing and disease. In parallel, we are developing novel anti-tumourigenic oxysterols that target a specific cellular pathway, the hedgehog (Hh) signalling pathway, which is involved in many cancers (most importantly pancreatic ductal adenocarcinoma).

Why has the therapeutic potential of oxysterols been overlooked in the past?

For many decades, all oxysterols were thought to possess similar qualities and activities. My colleagues and I were the first to perform extensive structure-activity relationship studies to demonstrate that, just as not all proteins or carbohydrates are the same, oxysterols also vastly differ in their biological activities and the responses that they elicit in their target cells. These can range from cytotoxic effects to an impact on stem cell differentiation. The field of oxysterol biology now recognises that, by making small changes in the molecular structure of the molecules, one can greatly influence their properties.

How did you come to found MAX BioPharma?

I started MAX BioPharma following my lab’s original discovery that specific naturally occurring oxysterols have potent osteogenic effects and, therefore, their more potent novel analogues may serve as therapeutic candidates for the treatment of osteoporosis and stimulation of bone healing. It quickly became clear that the successful development and commercialisation of this discovery would require far greater resources than what my academic lab at UCLA could provide, and that an enhanced focus on development toward commercialisation was necessary. Driven by a passion to find a cure for osteoporosis, having witnessed its devastating
and more potent analogues of oxysterols with osteogenic activity; secondly, demonstrating their ability to induce robust bone formation in vivo in animal models of spine fusion and cranial bone repair; and thirdly, by identifying strategies to produce bone-targeted osteogenic oxysterols for systemic administration and intervention in osteoporosis.

The company has created a comprehensive and detailed clinical development plan that will result in the filing of an Investigational New Drug (IND) application with the US Food and Drug Administration (FDA) for an osteoporosis therapeutic in the next 24-36 months. In addition, MAX BioPharma has successfully brought on board an experienced global commercialisation partner that will continue the development of a lead candidate as a therapy for the localised stimulation of bone formation in indications including spine fusion.

What do you hope to achieve in the next three to five years?

MAX BioPharma aims to initiate clinical trials for its lead anabolic agent for the treatment of osteoporosis. In parallel, the company will continue to develop anti-tumourigenic oxysterols, which it hopes to have in clinical trials for targeting malignancies that result from uncontrolled stimulation of the Hh pathway in the tumour microenvironment, beginning with pancreatic cancer.

In what way has MAX BioPharma’s research built upon this influential discovery?

MAX BioPharma has been able to expand the original discoveries by firstly producing novel and life-changing adverse effects on friends and loved ones, I started on the path of moving the technology from its academic home to an industry-focused company. To become better equipped to guide the initial steps of the company and provide a strategy to reach its objectives, I attended the Anderson School of Management at UCLA in 2010 and obtained an MBA focusing on entrepreneurship. As many agree, the passion of the entrepreneur and his or her belief in what the venture pursues is often fundamental to success!

LOW BONE DENSITY and osteoporosis increase risk of fracture and can be a cause of significant pain and disability, especially when the hip or spine is affected. Unfortunately, due to a rise in risk factors such as menopause, old age, diabetes and poor nutrition, incidence of osteoporosis is increasing. In the US, it is estimated that approximately half of all people over the age of 50 will have low bone density or osteoporosis by 2020.

Current prevention and treatment options for osteoporosis are almost exclusively focused on restricting further resorption rather than restoring bone that has already been lost. While one US Food and Drug Administration (FDA)-approved anabolic bone agent exists – Forteo (teriparatide) – it has several limitations: it must be administered daily via an injection, is associated with a number of unpleasant side effects, and is not always effective. As such, the development of novel drugs that are simple and cost-effective to produce and administer, and are capable of restoring bone density in a way that is effective and safe, would likely have a huge impact on reducing the burden associated with osteoporosis.

A GROUNDBREAKING DISCOVERY

In California, USA, the scientists behind biotechnology startup MAX BioPharma are...
producing novel and more potent analogues of oxysterols with osteogenic activity, while simultaneously setting up MAX BioPharma as a way to facilitate the efficient transfer of their findings from bench to bedside.

The MAX BioPharma scientists are now conducting research aimed at developing and testing novel osteogenic oxysterol analogues. They have so far produced two classes: one to stimulate bone formation locally (for orthopaedic procedures such as spinal fusion and fracture repair) and another to stimulate bone formation systemically (for osteoporosis). The former class has already been shown to produce positive results in vivo. “MAX BioPharma demonstrated robust stimulation of bone formation when its lead osteogenic oxysterols were administered in indications requiring localised bone formation, including spine fusion and repair of craniofacial defects in rats and rabbits,” Parhami outlines.

MAX BioPharma has conducted pioneering research in the emerging field of lipidomics since it was established in 2010. The researchers have a particular interest in oxysterols and the development of oxysterol-based therapies for osteoporosis.

**DEVELOPMENT OF OXysterols FOR STIMULATION OF BONE FORMATION AND INHIBITION OF TUMORIGENESIS**

**OBJECTIVE**

To leverage knowledge of small molecule oxysterols to create the next generation of therapeutic agents for intervention in some of the most fatal and debilitating human disorders.

**KEY COLLABORATORS**

Dr Michael E Jung, University of California, Los Angeles (UCLA), USA

Dr William Matsui, Johns Hopkins Institute, USA

**FUNDING**

National Institutes of Health, USA

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**Dr Farhad Parhami** obtained his BSc in Biology from UCLA in 1989 and his PhD in Experimental Pathology from the Department of Pathology under the mentorship of Dr Judith Berliner in 1994. He obtained a faculty position at UCLA in 1996 and initiated his research studies in bone and cardiovascular disorders. Parhami currently holds the title of Professor of Medicine at the David Geffen School of Medicine. He founded MAX BioPharma Inc. in 2010 and negotiated an exclusive license agreement from UCLA for the intellectual property involving a novel oxysterol technology platform developed in his laboratory. Parhami has been successful in developing MAX BioPharma into a fully functioning biotechnology company that performs R&D in three major clinical programmes that utilise novel oxysterols as therapeutic candidates.

**ANTICANCER OXysterols**

MAX BioPharma’s investigations are not limited to bone formation; indeed, the researchers have discovered that oxysterols may hold the key to several other serious disorders. Notably, while some oxysterols can serve as positive regulators of Hh signalling to stimulate bone regeneration, others can serve as negative regulators for the inhibition of tumourigenesis. For the MAX BioPharma scientists, it is simply a matter of altering their molecular structure. “Oxysterols are a class of signalling molecules in the human body that, unlike traditional hormones, neurotransmitters and growth factors, has been understudied – until recently. Our team at MAX BioPharma is extremely excited about investigating the remarkable biological properties of oxysterols. At the molecular level, we want to identify key structural features that are critical for new medical applications in orthopaedic medicine and cancer,” states Dr Frank Stappenbeck, Director of Chemistry at MAX BioPharma.

This finding has led to a series of preclinical studies aimed at determining the usefulness of this new class of oxysterols as a potential cancer therapy, particularly for the treatment of blood malignancies and pancreatic cancer. So far, MAX BioPharma scientists, in collaboration with Dr William Matsui at Johns Hopkins Institute, USA, have successfully demonstrated the ability of these oxysterols to block the growth of pancreatic cancer cells, and inhibit aberrant Hh pathway signalling in tumour cells, multiple myeloma and leukaemia cells.

MAX BioPharma is currently carrying out research in collaboration with scientists at the Johns Hopkins Institute to further advance understanding in this area. Ultimately, MAX BioPharma hopes to develop novel, effective cancer therapies capable of reducing or preventing tumour growth and metastasis in various types of cancer, which can be used either alone or in combination with other therapies, and which have fewer side effects than conventional chemotherapy.

**THE ROAD TO DRUG DEVELOPMENT**

While MAX BioPharma has already made significant preclinical progress in a relatively short space of time, its researchers are well aware that the road towards drug development and commercialisation will be littered with obstacles. One of the most important challenges ahead will be that of ensuring the safety of their novel drugs. “Long-term use of anti-resorptive agents has been shown to produce serious adverse effects, and there have been concerns regarding the formation of bone tumours in rats following the administration of Forteo,” Parhami expands. “This raises the importance of close monitoring as other bone anabolic agents are developed.”

Nonetheless, MAX BioPharma scientists plan to begin clinical trials for their lead anabolic agent for the treatment of osteoporosis within the next three to five years, and hope that clinical trials involving their anti-tumourigenic oxysterols as a treatment for pancreatic cancer will not be far behind. The company has also recently partnered with a global commercialisation partner to advance development of their therapy for the localised stimulation of bone formation.

The promising preclinical results and innovative nature of MAX BioPharma’s platform technology – of the few other candidate bone anabolic agents in preclinical and clinical development, no others are based on lipids – have already attracted significant interest and support, both from the pharmaceutical industry and the US National Institutes of Health (NIH). Moving forward, Parhami is confident that MAX BioPharma will become a key player in the emerging field of oxysterol-based therapeutics. “MAX BioPharma is the pioneer and leader,” he states. “With its strong intellectual property portfolio and extensive trade secrets, it is positioned to bring groundbreaking discoveries from bench to bedside, targeting unmet medical needs and significant markets.”