BREAKING GROUND

THE FOUNDATIONS FOR MEDICAL PROGRESS

SPECIAL FOCUS
Key contributors offer their take on the greatest barriers to research excellence

EXCLUSIVES
American Society for Reproductive Medicine
Canadian Partnership Against Cancer
National Alliance on Mental Illness
Canadian Lung Association

RESEARCH SPOTLIGHT
Canadian Cardiovascular Society
Ontario Chronic Disease Prevention Alliance
A sustainable future for lung research

Describing his collaborations with committed and expert colleagues in the field of lung research, world-class researcher Joe G N 'Skip' Garcia, MD discusses how his work is advancing the field of pulmonary medicine.

As an internationally recognised physician-scientist, policy advisor and general polymath, how do you effectively balance your time between various commitments?

In this type of academic leadership position you are only as good as the quality of the people around you. In my prior leadership roles I have been fortunate to be at the head of great teams. Now, at the University of Arizona (UA), I am building another high-quality and talented academic leadership group that will ensure profound synergy and success in promoting our tripartite academic mission of health education, clinical care and research.

I am passionate about biomedical research and discovery and have always believed that one leads by example. Therefore, managing my laboratory research programme that has been continuously funded by the National Institutes of Health (NIH) for the past 30 years, providing mentorship to both aspiring young investigators and seasoned department heads, and leading strategic initiatives to advance the quality and cost effectiveness of our patient care programmes are all important activities, both to me personally and to the success of the UA health sciences.

What important results emerged from your recent study investigating the relationship between blood cell gene expression and outcomes in patients with idiopathic pulmonary fibrosis (IPF)?

IPF is a fatal lung disease characterised by scarring of the lung from an unknown aetiology that has different progression rates. No therapy is available for IPF except lung transplantation, which is highly limited by donor lung availability. Median survival rate is 3.5 years, so providing patients with an accurate prognosis is critical. We employed a genome wide study using blood cells from IPF patients, which is less invasive than obtaining lung biopsies, and identified an expression profile that correlates with transplant-free survival. The gene profile predicts disease severity and provides clinicians with information on the priority and urgency of lung transplantation.

How does your research facilitate the development of new strategies and targets to limit the adverse effects of injured pulmonary circulation?

The pulmonary field has many unmet medical needs since many diseases have limited...
Therapeutic options and unacceptably high mortality rates. The research strategies utilised by my lab have not only identified several novel biomarkers and targets, but also provide a blueprint for other investigators to employ genomic approaches and discover new targets. These approaches are the foundation upon which modern investigators will incorporate their research and develop the tools clinicians need to practise personalised medicine.

Can you reveal your plans for advancing the Arizona Health Sciences Center (AHSC) and expand on the areas of excellence?

We're recruiting nationally-noted physician-scientists and scholars to help lead our efforts to advance and develop AHSC by expanding research and clinical care. In December 2013, I convened advisory councils in four key research areas: Health Disparities; Precision Health; Neuroscience; and Population Health and Health Outcomes. Drawing faculty members from across both the Tucson and Phoenix campuses, and involving 11 UA colleges, the councils are charged with evaluating our internal strengths and weaknesses as well as outside threats and opportunities in their respective areas. Each council will provide recommendations to advance AHSC’s distinction and national reputation. This will strategically strengthen and expand our basic, clinical, and translational research programs and improve our position in the hyper-competitive environment for federal research funding.

As a world-class researcher and the recipient of many prestigious awards, what is your proudest achievement to date?

I would say either my community service award from the State of Indiana for my work illuminating the health challenges of migrant farm workers while I was at Indiana University, or the recognition by my academic peers, nationwide chairs of departments of medicine, for my success in implementing novel strategies to increase diversity in an academic department of medicine.

Looking ahead, can you discuss your vision for your research over the next decade?

In the post-human genome era, identifying strategies that deliver precision health, high-quality outcomes and cost-effective therapies is a necessity given the challenges of the healthcare reform environment. I endeavour to be a leader in implementing precision medicine tactics in the critical care setting. This trend toward personalised or individualised medicine will continue to dominate healthcare over the next decade.
INTELLIGENCE

CYTOSKELETAL REGULATION OF LUNG ENDOThelial PATHOBiology

OBJECTIVES
To develop novel therapies for critically ill patients with acute inflammatory lung disease.

KEY COLLABORATORS
Viswanathan Natarajan, PhD; Steven M Dudek, MD; Jeffrey R Jacobson, MD, University of Illinois, Chicago • Augustine M K Choi, MD, Cornell Medical College • Ivan O Rosas, MD, Harvard Medical School • Laura L Koth, MD, University of California, San Francisco • Naftali Kaminski, MD, Yale University

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CONTACT
Joe G N ‘Skip’ Garcia, MD
UA Senior Vice President for Health Sciences
University of Arizona
Arizona Health Sciences Center
Drachman Hall
1295 N Martin Avenue
Tucson
Arizona, 85721
USA
T +1 520 626 1197
E skippgarcia@email.arizona.edu

WITH THIS UNDERSTANDING, THE TEAM NOW HOPES PHYSICIANS CAN DEVELOP DIFFERENT THERAPEUTIC AND MANAGEMENT STRATEGIES FOR TREATING HIGH-RISK BLACK PATIENTS. WHILE THIS RESEARCH IS INVALUABLE FOR MANAGING ARDS IN A RANGE OF COMMUNITIES, IT ALSO SERVES TO HIGHLIGHT THE CHALLENGE OF PERSONALISING HEALTHCARE. MANY CLINICAL TRIALS FAIL TO DISTINGUISH BETWEEN SEX, RACE AND OTHER KEY GENETIC DETERMINANTS, LEADING TO UNDERSTANDING OF COMORBIDITY AND GENDER-BASED DIFFERENCES IN DISEASE AND TREATMENT EFFICACY DESPERATELY LACKING.

MINIMISING TREATMENT RISK
Garcia and his colleagues are also investigating the impact of treatment and management for lung disease and the assessment of risk versus benefit in these various strategies. One area of interest the researchers have focused on is the initiation of local inflammatory responses in the lung due to mechanical ventilation: “Critically ill patients with respiratory failure are placed on mechanical ventilation as a lifesaving supportive therapy,” Garcia highlights. Unfortunately, the process itself can stress the lung endothelium, stimulating the release of pro-B cell colony-enhancing factor (PBEF), which acts as a chemical signal that triggers localised inflammation. This process amplifies lung inflammation and is potentially damaging. Garcia has worked to create monoclonal antibodies with the specific structure to target and inactivate PBEF, thus reducing both inflammatory responses and the risk of comorbidities in these already critically ill patients. Today, monoclonal antibodies are being developed by Aqualung Therapeutics, a company established by Garcia, for the treatment of ventilator-associated lung injury.

The work at the UA that falls under the umbrella project, concerned with the cytoskeletal regulation of lung endothelial pathobiology serving to improve understanding of disease and genetic predictors in the field, and also highlighting the challenges of improving evidence-based personalised healthcare in modern clinical practice. Investigation into the pathology of lung disease demands an intelligent and sustained model of research supported by committed experts and considerable funding. Programmes meeting all of these criteria are few and far between and the work being conducted by Garcia and colleagues should be celebrated as a success in this context, and also emulated as a model of best practice for a holistic approach to research that simultaneously endeavours to promote ethnic and social diversity in the academic and medical professions.