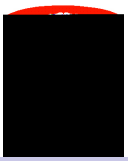
# VITAL SIGNS



# Polygenic Risk Scores

Shawn Bradley is a tall guy. At 7 ft 6 in, he's one of the tallest players in the history of the NBA. Watching him play for the Philadelphia 76ers, most clinicians would suppose that he has acromegaly, or a rare genetic base pair mutation leading him to be tall. But he has neither. In fact, when his genome was sequenced, he was found to simply have an extreme accumulation of the genetic alleles that are commonly found in the population to be associated with being tall. In the world of modern genetics, we'd say that Shawn Bradly has a "high polygenic risk" for being tall. Over the past 12 months, it's become apparent that we can start to identify people in the population who have a high polygenic risk for many diseases. And this information may be clinically useful.

Polygenic risk scores are simple. At their core, they are just a sum of the alleles that predispose to a disease. These can be summed for each person in a population and then that population can be stratified for those at high and low risk of disease. At present, most such scores rely upon common genetic determinants of disease, which we call SNPs (single nucleotide polymorphisms). Since natural selection has allowed these SNPs to become common in the population, individually, they have a small risk of disease. But by adding up tens of thousands, or perhaps millions of these variants, we can start to identify people at reasonably high risk of disease.

What is clinically attractive about these risk scores is that they seem to be generally uncorrelated with most known risk factors. So, for example, when we predict people with low bone density from a polygenic risk score, we are adding information that is independent of known risk factors. This enables better risk stratification. Further, the number of people at high risk can be large. For example, using a polygenic risk score, colleagues at Harvard have identified 8% of the European-ancestry population that has a ~3-fold increased risk of coronary heart disease. To put this in perspective, type 2 diabetes imparts a 2-fold risk of coronary heart disease and affects 8% of the population.

Many questions need to be resolved prior to clinical application and these include costs of genotyping, storage of information, ancestry-specific effects, changing physician and patient's behaviour and regulatory concerns for new diagnostic tests. We and others are working on these questions now.

But in the mean-time, k r m' hangiŐ M p n ] ⁎ l sh rh _ a я ! ti W ³ m ti y

# Fertile Ground:
# Women's Immunology at the MUHC

November 1st 2017,

Hello from Bordeaux! I'm writing this while nearing the end of my sabbatical stay at Bordeaux University, where I have had the privilege to hold the position of an Initiative d'excellence (IdeX) Visiting Scholar through two consecutive IdeX awards in 2017 (July-Dec) and 2018/2019 (Sept-March). My host was the ImmunoConcEpT Laboratory, a superb team of fundamental and clinical immunologists who collaborate flawlessly to solve clinical problems or understand clinical observations

Director of the Division of Radiation Oncology at the MUHC since September 2015. In this role, he has introduced a number of efficiencies and innovations for the care and flow of patients in

# RETIREMENT

**Barry Posner** grew up in Winnipeg and experienced the challenging environment of cold weather and a tough neighborhood. Strong, determined and incredibly intelligent he thrived despite the challenges. He completed medical school at the University of Manitoba followed by residency training and a Metabolism fellowship at the New England Medical Center in Boston, and pursued a research postdoctoral fellowship at the NIH in Biochemistry. He came to McGill in 1970 and has had a most distinguished career, replete with notable accomplishments. His contribution to research, education and administration has been recognized in Quebec, Canada and internationally. Some of the most noteworthy honors are election to the American Society of Clinical Investigation, the American Association of Physicians, the Royal Society of Canada, an officer of the Order of Canada and a member of the Canadian Academy of Health Sciences. He was awarded the Distinguished Scientist Award from the Canadian Society for Clinical Investigation. He has been invited to present

# RETIREMENT

**Jim Stewart** became a cardiac

**Dr. Tricia Peters**, Assistant Professor to the Division of Endocrinology & Metabolism and Attending of the Jewish General Hospital. Dr. Peters earned her M.D. at SUNY Stony Brook University, Stony Brook, New York and obtained her PhD from the University of Cambridge, Boston. She completed her post-graduate training in internal medicine and adult endocrinology and metabolism at McGill University. Dr. Peters will have clinical duties at the JGH, where she will be involved in teaching students and supervising medical residents. She will continue to advance her research in the field of diabetes.

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