**30 plus 10 Q&A**

**Mutational signatures: What caused the mutations in these cancers? Why do we care?**

Mutational signature analysis looks for patterns of somatic mutations with the ultimate aim of deducing what caused the mutations. Mutational signatures are important for understanding DNA damage and repair, for understanding the cellular origins of cancer, for detecting mutagenic exposures that cause cancer, and for preventing and treating cancer. Aristolochic acid, a mutagen found naturally in herbs that are widely used as medicine, is a straightforward example. In the last 7 years, mutational signatures have implicated aristolochic acid as a common cause of liver, urinary tract, and oesophageal cancers. More involved analyses require machine learning, which can infer mutational signatures from the mutations in large numbers of cancers. Multiple approaches for this have been developed, but the process still requires substantial human guidance and interpretation. Furthermore, existing approaches are poorly-suited to answering common questions, such as “Does this set of tumours contain any novel mutational signatures?” and “What is the evidence that a particular signature is present in a given tumor?” I will propose some new computational approaches to answering these questions.

**Steven G. Rozen, PhD**

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Steve Rozen's research has spanned bioinformatics, human genetics and cancer genomics. Rozen founded and directs the Duke-NUS Centre for Computational Biology, which has published > 250 scientific papers since 2013. Rozen's own laboratory focuses on bioinformatics and cancer genomics and has been part of a team-science effort in cancer genomics that led to multiple papers, including 5 in *Nature Genetics.* This research was recognizedby theAmerican Association for Cancer Research (AACR) 2018 Team Science Award and the 2015 Singapore President's Science Award. Within cancer genomics, the Rozen lab studies alternative splicing, lncRNAs, and mutational signatures as tools for studying cancer (<https://www.nature.com/articles/s41586-020-1943-3>). Rozen also created and maintains the widely-used Primer3 software for PCR primer design. Previously, he studied rearrangement mutations in human Y chromosomes and their clinical consequences*.*

(Pictures below; please use the version of the picture that you prefer…)

