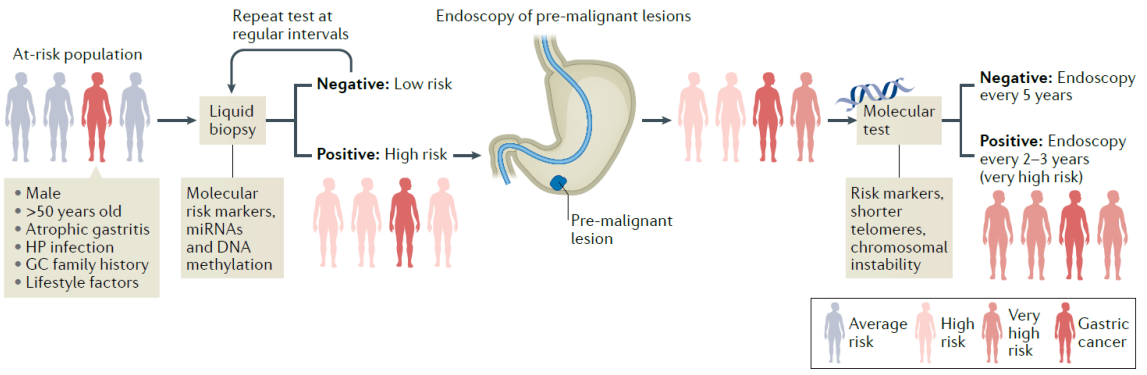
MAPPING THE GENOMIC DIASPORA OF STOMACH CANCER



Precision prevention strategies for GC. *In regions of low and intermediate gastric cancer (GC) risk, endoscopic screening for all-comers is cost prohibitive. Pre-screening of 'at-risk' populations based on clinical criteria (male, older age) and molecular blood tests for early GC detection (microRNA (miRNA)/DNA methylation-based liquid biopsies) may identify 'high-risk' individuals who will benefit from endoscopic screening. Surveillance of patients with pre-malignant conditions, such as intestinal metaplasia, using molecular tests detecting copy number alterations and reduced telomere lengths may also prove useful in stratifying 'very-high-risk' individuals for intensive and repeated endoscopic follow-up. HP, Helicobacter pylori.*

Cancer of the stomach (aka gastric cancer, GC) is a major cause of global cancer mortality, being responsible for >700,000 deaths annually. Particularly prevalent in Asia, Africa, and developing countries, most GC patients are diagnosed with late-stage disease, with current treatment strategies still largely based on "one-size-fits-all" regimens and only a few biomarkers currently approved to guide treatments. There is thus an urgent need to identify new molecular pathways driving the development of GC, as such information may provide opportunities for preventing GC, facilitate early GC detection, refine the use of existing treatments and identify novel targets for new GC therapies.

In this *Nature Reviews Cancer* review, Profs Yeoh Khay Guan (National University Health System, NUHS) and Patrick Tan (Genome Institute of Singapore, GIS, and Duke-NUS Medical School Singapore) from the Singapore Gastric Cancer Consortium provide a comprehensive update of recent genomic and epigenomic studies of GC, and how these findings improve our basic and foundational understanding of GC. This Review is a follow-up to the same authors' previous 2015 authoritative review published in the leading clinical journal *Gastroenterology*.

Building on pioneering genomic studies in the earlier half of the decade from major consortia and also from the Singapore team, the current review summarises new findings in GC. It covers the identification of molecular aberrations affecting the non-coding genome, epigenome, and transcriptome, and how these events can both drive GC-related processes and also harnessed to guide therapy selection.

The review also covers emerging technologies for studying GC including single-cell platforms, liquid biopsies, proteomics, and metabolomics, which are deepening our understanding of GC heterogeneity both between-patients and within-the-same patient, further yielding promising new pre-clinical targets.

Finally, the review surveys recent work examining both terminal ends of the GC lifecycle, from pre-malignant lesions to distant metastases, and how this information could be exploited for cancer prevention and the realisation of GC precision oncology.

This review was published in *Nature Reviews Cancer* on 26 October 2021.

"This Review provides a timely summary of the most up-to-date findings in the area of gastric cancer (epi)genomics, a serious disease condition highly prevalent in Asia and relevant to many Asian populations including those in Singapore. "

Prof Patrick Tan, Executive Director, GIS