KEYNOTE TALK

Wednesday, October 13, 2021 at 9am

Barrett's Esophagus: efficient design of multiscale simulations for surveillance and treatment

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Abstract: Barrett's Esophagus (BE), a metaplastic tissue alteration associated with gastroesophageal reflux, predisposes to esophageal adenocarcinoma (EAC). Endoscopic screening of patients with persistent symptomatic reflux aims to identify patients with BE at risk of progressing to cancer. Such patients are recommended to undergo follow-up examinations for dysplasia or small cancers in the earliest stages. This is useful because the prognosis for EAC detected at an early stage is dramatically better than for advanced stages that are mostly lethal. Thus, endoscopic surveillance of BE, in which multiple biopsies are routinely examined for preneoplastic changes and/or early neoplastic lesions, will increase patient survival compared with patients diagnosed with EAC without prior BE surveillance. However, over-diagnosis is a major concern because the annual rate of progression from BE to EAC is less than 1% overall but depends on age, gender, race/ethnicity, BE segment length, history of gastroesophageal reflux and other life-style factors. Multiscale models that include these factors have been developed but suffer computational bottlenecks and are technically demanding. In this talk I will discuss how mathematical insights and multitype branching process theory can be used to significantly speed up simulations to assess and evaluate various screening modalities in a large number of individuals.

Speaker Bio-Sketch: Georg Luebeck is a member in the Herbold Computational Biology Program at the Fred Hutchinson Cancer Research Center and Affiliate Professor in Applied Mathematics (University of Washington). Inspired by the pioneering work of Moolgavkar, Venzon, and Knudson (MVK), he has made significant contributions to stochastic models of cancer and its precursors based on principles of multistage carcinogenesis. Among them, the development of mathematical and computational tools to facilitate the application of stochastic multistage clonal expansion (MSCE) models to cancer screening, intervention, and prevention, in particular for colorectal cancer and esophageal adenocarcinoma. His recent work focuses on age-related epigenetic drift and its impact on aging and cancer development in colon and esophagus. In Luebeck et al., Cancer Res. 2019 vol 79(3), he explored the implications of epigenetic drift in colorectal tissues and its potential role as a selective force in neoplasia. Similarly, he and his colleagues identified significant effects of differential epigenetic drift in Barrett's esophagus (BE) associated with biological tissue aging and silencing of genes that are known to repress endogeneous retroviruses.