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Biography

Yusuke Yamamoto has completed his PhD in Molecular Physiology from Waseda University in 2008 and postdoctoral studies under Prof. Frank McKeon and A/Prof. Wa Xian at Genome Institute of Singapore. He has been interested in how adult stem cells maintain their stemness throughout the lifespan as well as identifying cell-of-origin in esophageal adenocarcinomas and high grade serous ovarian carcinoma, which are most aggressive type of cancers with poor prognosis. He has published more than 40 papers in reputed journals, including Nature and Cell.

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**CLONING BARRETT'S
STEM CELLS SUGGESTS
PATHS TO INITIATION OF A
PRECANCEROUS LESION**

Stem cell populations of columnar epithelia collectively resist cloning in their immature states. By modifying the culture technique for human intestinal stem cells, we have cultured the stem cells from precancerous lesion known as Barrett's esophagus which is intestinal metaplasia, emerged from a squamocolumnar junction and would eventually evolve to esophageal adenocarcinoma. Here we report the isolation and propagation of distinct, patient-matched stem cells of Barrett's, gastric and esophageal epithelia that yield divergent tumor types following *in vitro* transformation and xenografting. Exome-seq revealed a broad mutational spectrum unique to Barrett's stem cells that likely reflect the risk for oncogenesis. Remarkably, 25% of cases show no cancer-related genomic changes, suggesting that Barrett's initiates without driver mutations. Most cases, however, sustain patterns of deletions almost identical to adenocarcinoma. Notably, those suspected of low-grade dysplasia have p53 mutations or undergo amplifications of proto-oncogenes and receptor tyrosine kinases, implicating these events in lethal transitions. Our findings suggest paths for the initiation and progression of Barrett's esophagus and define a discrete stem cell underlying its regenerative growth whose eradication could prevent esophageal adenocarcinoma.

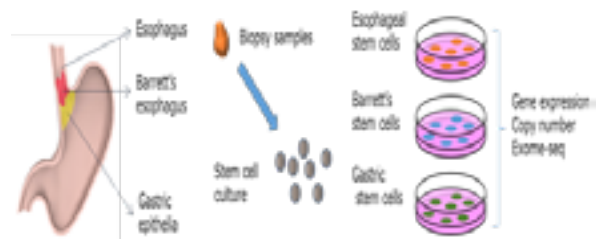


Figure1: A strategy for the stem cell culture of Barrett's, esophagus and gastric stem cells



Note:

Related Publication

Yusuke Yamamoto, Xia Wang, et al., (2016) Mutational spectrum of Barrett's stem cells suggests paths to initiation of a precancerous lesion. Nature Communications. 7: 10380