UC San Diego
MOORES CANCER CENTER

2020 Cancer Control Program Pilot Project Award

Diagnostic Biomarkers of HCC Using Microbial DNA

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Scientific Abstract:

The current methods of detecting hepatocellular carcinoma (HCC) are costly and inadequate. Therefore, there is a *critical need* for better diagnostic markers to improve HCC screening and surveillance and decrease cancer-related mortality. The *overall goal* of this proposal is to find a biomarker for the early detection of HCC using tumor resident bacteria. This proposal is born out of preliminary data from our collaborator, Rob Knight, that indicate that DNA from tumor-dwelling microbes can identify malignancies. Approximately 2.5% of reads in The Cancer Genome Atlas (TGCA) are microbial. Machine learning algorithms using these microbial reads accurately identified solid tumors from each other and from adjacent control tissue. This preliminary data is particularly robust for HCC. Thus, our *central hypothesis* is that tumor-associated microbial DNA could be used in diagnosis and treatment guidance of HCC. In the next year, we will pursue our central hypothesis in one aim. We will use the machine learning algorithms developed from TGCA on a new cohort of samples from the University of Florida liver biobank. This biobank has nearly as many HCC samples as the entire TGCA network. Thus, the proposed studies will help determine whether the machine learning algorithms developed from TCGA can detect whether HCC has been treated (e.g. chemoembolization) and thus potentially serve as a tool for surveillance. If successful, a similar strategy can be used to investigate additional cancers that lack poor rveillance biomarkers, such as cholangiocarcinoma and pancreatic cancers, and thus lay the foundation for future R01 grants.

Lay Abstract:

Hepatocellular carcinoma (HCC) is the fifth most common tumor worldwide and the second most common cause of cancer-related deaths. Only one person in five lives past five years once they are diagnosed with HCC. This is mainly because HCC is usually detected at an advanced stage, when there are a limited number of therapeutic options. Recently, we've learned that there are bacteria that can live inside cancer tissue. The dead cells and lack of oxygen in tumors are particularly good environments for bacteria to grow. One of our collaborators analyzed The Cancer Genome Atlas, a huge database containing the genetic sequences of different cancers, and found that ~3% of these sequences actually belonged to bacteria. To determine whether each cancer had its own set of bacteria, his team trained a computer to learn which bacterial sequences were linked to each particular cancer. When this computer was given a test on new cancer tissue sequences, it was amazingly accurate in distinguishing between different cancer types based on what it had learned from the bacterial sequences. Moreover, it was particularly good at distinguishing HCC. This made us interested in determining whether we can use bacterial sequences in HCC tumors to learn more about this cancer and to find new ways to diagnose it at a much earlier, more treatable stage.