## Biological Design Doctoral Defense

An Evolutionary Perspective on Neoplastic Disease Across the Tree of Life

School for Engineering of Matter, Transport and Energy

Valerie Harris

Advisor: Carlo Maley

## **Abstract**

Cancer is a disease of multicellularity, with dee evolutionary origins. As such, the forces of both evolution and natural selection operate on multiple scales to govern tumor dynamics. As multicellular organisms increase in complexity, cellular-level fitness must be controlled in order to maintain organismal-level fitness. Mutations that might provide a benefit at the cellular level by allowing for rapid proliferation are subject to the same forces that function on the organismal level, wherein cancer suppression is a benefit – especially as organisms increase their body size and lifespan. In order to maintain these large cellular bodies and long lifespans, organisms must increase their means of cancer suppression, and it is likely that these two phenomena co-evolved together. On a smaller scale, the cooperative dynamics of circulating tumor cell (CTC) clusters engage in cooperation to form networks of connected single cells that provide protection, stability, and cooperative sharing of resources to enhance their survival as they detach from a primary tumor and metastasize at secondary sites. This work seeks to explore the phenomenon of multi-level selection in neoplastic disease by examining A) the mechanisms of cancer suppression at multiple scales, B) the ecological resilience and stability of cooperating cellular clusters and C) a largescale dataset on cancer prevalence across mammals, sauropsids (birds and reptiles), and amphibians, illuminating the evolutionary life history characteristics that explain the tradeoffs between cancer suppression and overall organism fitness. By taking an ecological and evolutionary approach to understanding cancer, novel strategies of cancer treatment may be discovered alongside fundamental discoveries about the fundamental forces of selection that govern evolutionary dynamics from the cellular to the organismal scale.