Mechanistic Modeling to Identify the Age-associated Variation in the T Cell Compartment in Head and Neck Cancer Patients

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Fas^+ expression is enriched in the peripheral circulation of $CD4^+$ and $CD8^+$ T cell populations of head and neck cancer patients (HNC). The abnormally high percentage of Fas^+ expression in $CD4^+/CD8^+$ T cells were observed to increase in circulating T lymphocytes from HNC patients, and to a more extreme degree in healthy individuals (controls). As the proportion of Fas^+ expressed accrues with host age, the percentage of Fas^- will correspondingly deplete, progressively reversing the ratio of Fas^+:Fas^- in the T cell pool. The mechanisms that drive this fractional upregulation of Fas^+ on $CD4^+/CD8^+$ T cell repertoire remain elusive. To extend our knowledge further, we will develop a mathematical modeling framework to identify cellular processes that regulate the age-associated accumulation of Fas^+ T cells using previously published data. Assuming that the age-induced increase in of Fas^+ expression is mediated by cell intrinsic factors, we consider a substantial disparity in loss rates between Fas^+ and Fas^- cells, suggesting kinetic heterogeneity within a T cell population. Alternatively, we define a model with an age-dependent increase in the rate of conversion from Fas^- to Fas^+ T cells, driven by aging related changes in the tissue environment. We will statistically validate and compare the ability of these models to delineate the data in pursuance of understanding the dynamics of Fas expression in both $CD4^+$ and $CD8^+$ T cells. Pinpointing the mechanisms that govern the age-related increase in Fas^+ expression in the T cell population, may provide a strong foundation for the target discovery and thus may augment the potency of immunotherapeutic interventions against malignancies associated with head and neck cancer.