Modeling contact inhibition of growth using multi-cell modeling platform Compucell3D

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Contact inhibition is a fundamental mechanism by which cells arrest their growth when they come into contact with each other. The underlying cell property that brings about contact inhibition is cell-cell adhesion, which is achieved through homophilic cell adhesion proteins called cadherins. When intracellular cadherin localization is disrupted, cells become highly flattened with very little cell-cell contact. Cadherins also arrest or retard cell growth when overexpressed and increase secretion of growth factors, when disrupted. Cadherins seem to be fundamental in linking cell-cell contact and cell growth. Therefore, we hypothesize that the extent of cell-cell contact is a consequence of cadherin junctions and can be treated as a *constitutive property* that can control cell growth and proliferation. We have demonstrated this using Glazier-Graner-Hogeweg model implemented in a multicellular modeling platform Compucell3D to simulate cell growth. We present a mathematical formulation based on cell-cell contact area that allows individual simulated cells to make growth decisions based on local environment. We show that this approach can be effectively used to model contact inhibition of growth in confluent monolayers, re-growth of tissues in response to wounding and tissue morphogenesis. In addition to modeling these properties, we also mathematically reproduce a recent experimental result showing the opposing effects of growth factors and cell-cell adhesion molecules in establishing contact inhibition.