CDB SEMINAR

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16:00~17:00 C1F CDB Auditorium

Tumor cell dormancy and recurrence: a view from EMT

Summary

Contrary to the widely held view that the precursors of metastasis are derived from the most advanced clone within the primary tumor, it has become evident that tumors may disseminate even from the early phase of oncogenesis with a far less progressed genomic state. Such early-disseminated tumor cells may become dormant at sites of the metastasis, and after accumulating further genetic alternations and/or interacting with the microenvironment cells may then start their cancerous growth.

Inactivation of E-cadherin and activation of some integrins, a process resembling EMT, are a hallmark characteristic of tumor malignant development, and necessary for invasion and metastasis of most cancers. In the case of mammary tumors, a direct interaction network built around cancer CD44+ cell specific genes as well as mesenchymal profiles is centered around TGFβ1, while TGFβ1 alone is unable to induce EMT in normal mammary epithelia and mostly induces cell growth arrest.

We have identified an Arf6 pathway specific to breast cancer invasion and metastasis. This pathway was activated by growth factor receptor tyrosine kinases (RTKs), and has recently turned out to be crucial for the E-cadherin inactivation and the integrin activation, and hence appears to be closely related to the progression of cancerous EMT. A question then arisen was the relationship of the RTK-driven Arf6 pathway with the TGFβ1 signaling in induction of metastasis and on being stem cells of primary tumors of the human breast. Based on our data, we like to address the above mentioned outstanding question, that is, tumor long-term dormancy and re-growth within a niche that is not innate to the tumors. In this occasion, I like to discuss these points to which we are yet to have a clear way to approach.

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