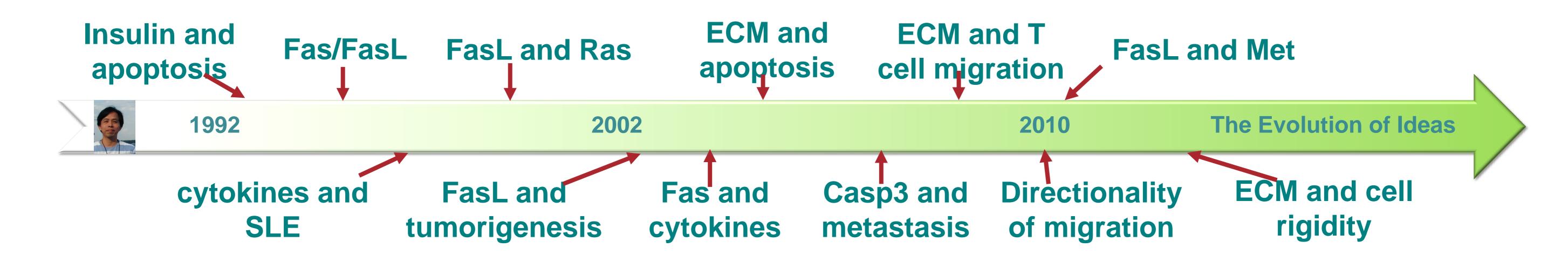
Output-lab For Tumor Microenvironment:

Studies on immune erosion

<u> 楊倍昌 (Bei-Chang Yang)</u>

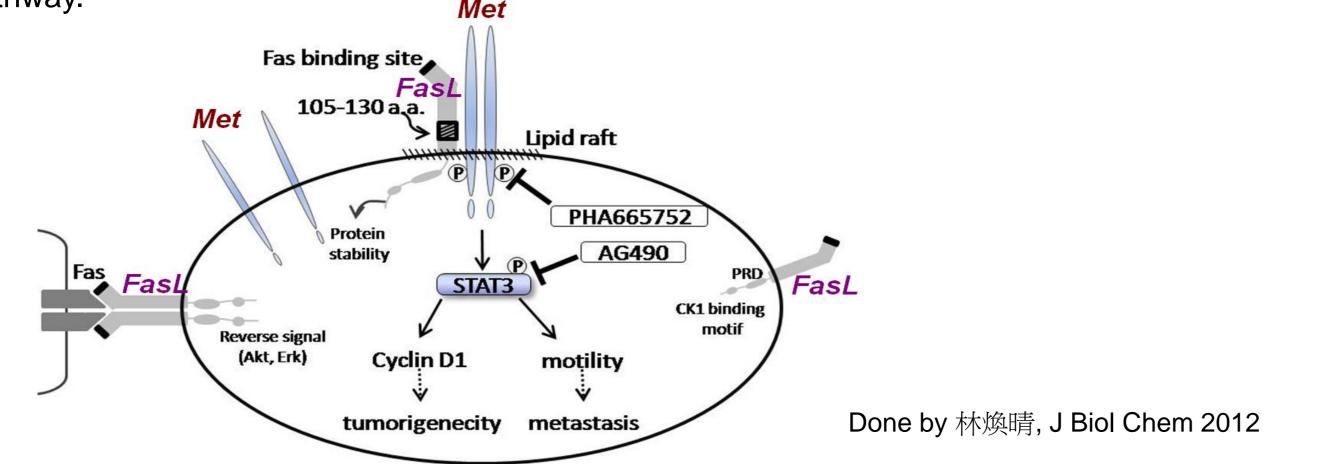




Novel signaling of FasL through Met

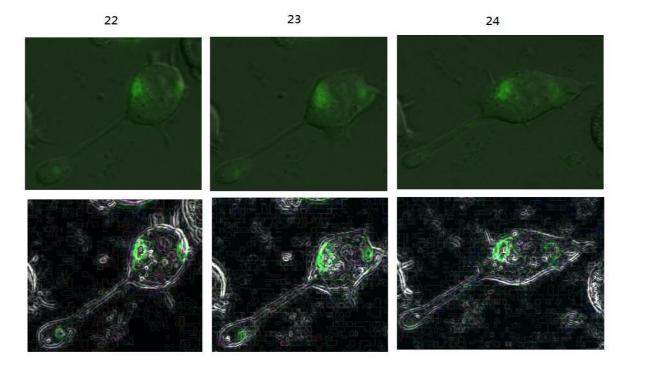
ZAP-70 appears at lamellipodia before protrusion

FasL can hijack the Met signal pathway to confer cells with an invasive phenotype. The activation of Met by FasL deletion mutants without intracellular domains represents a new paradigm for FasL signal transduction. This novel signaling mechanism explains the observation that high-grade FasL-positive tumors show elevated metastasis potential in a Fas-independent pathway.

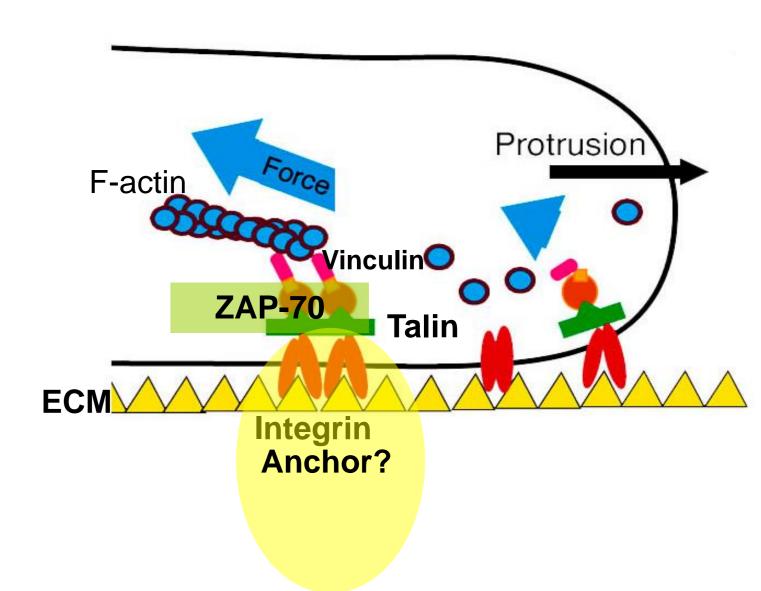


Tenascin-C prevents lamellipodia formation of T cells

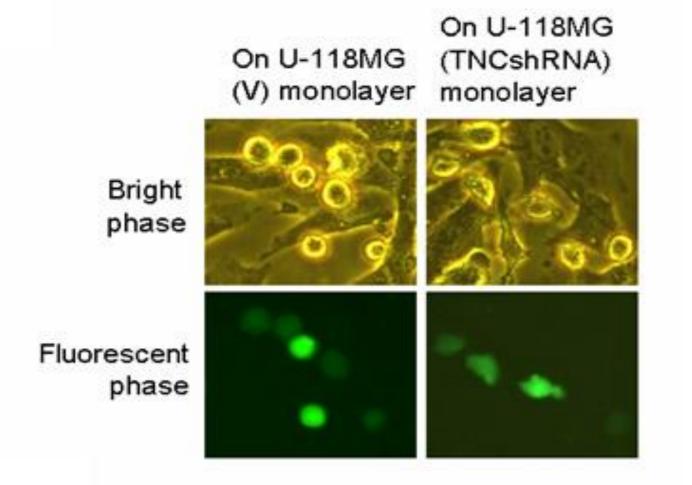
Migration-permissive ECM, such as fibronectin, engages the integrin a/b of T cells to activate ERK resulting in elevated actin polymerization and amoeba-like moving. This process will facilitate T cell infiltration into the tumor area. Tenascin-C secreted by glioblastoma to tumor stroma interferes the interaction of ECM and integrin that would blunt T cell migration.



Expression of ZAP-70-GFP (green) in migrating P116 cells. Images were taken by Cell-R microscopy. (Done by 吳佳芸, 2010).



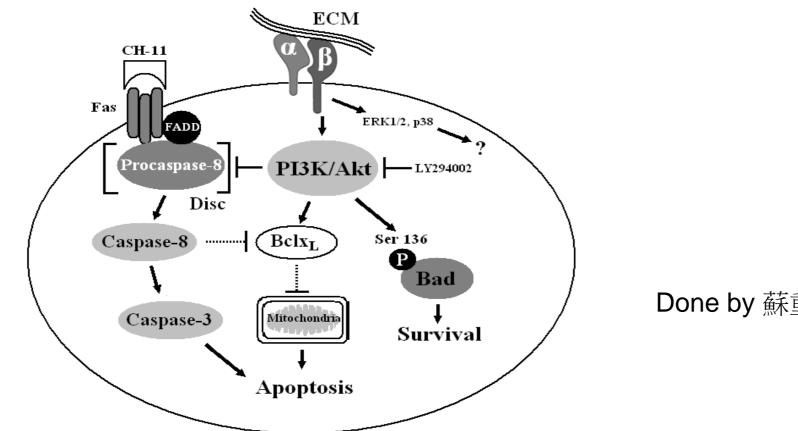
Fibroblast infiltration into tumor stroma



Done by 黃俊淵, J Immumol 2010

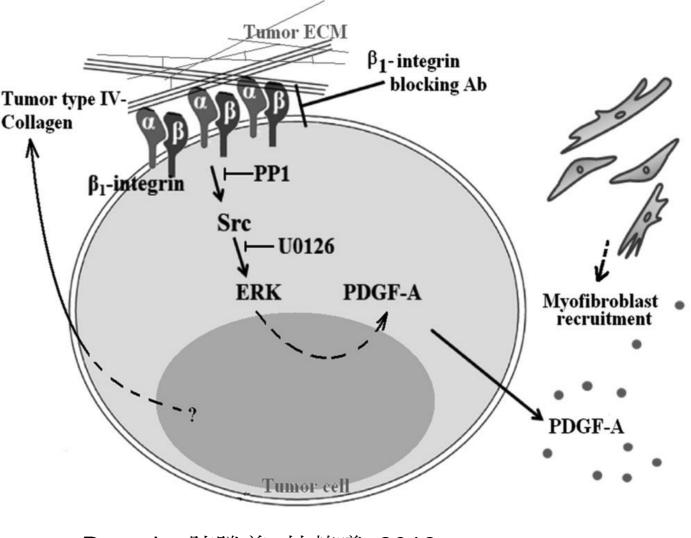
Integrin-signal suppresses T cell apoptosis

stimulation of the β integrin signal of T cells by contact with tumor cells may trigger a novel protective signaling through the PI3K/Akt pathway of T cells against Fas-mediated apoptosis.

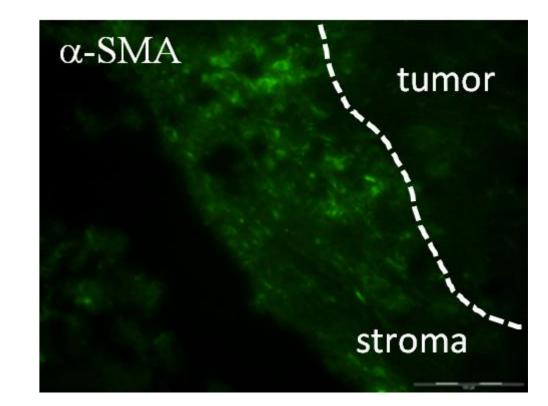


Done by 蘇重禎, J Immumol 2007

Proposed working model for tumor fibroblast infiltration initiated by the deposition of collagen through enhanced PDGF-A production.



Done by 陳勝義, 林若曦, 2013



α-SMA-positive cell infiltration in the stroma region of human glioma
 (immunofluorescence image)



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Selected publications

- Su CC, Lin HC, Lin YP, Shan YS, and Yang BC (2013) Expression of Th17-related genes in PHA/IL-2-activated human T cells by Fas signaling via caspase-1- and Stat3-dependent pathway. Cell Immunol.
 281:101–110
- Lin HC, Lai PY, Lin YP, Su CC, Huang JY, and Yang BC (2012) Fas ligand enhances the malignant behavior of tumor cells through interaction with Met, hepatocyte growth factor receptor, in lipid rafts. J Biol Chem. 287:20664–20673.
- Hwang JY, Cheng YJ, Lin YP, Lin HC, Su CC, Juliano R, and Yang BC (2010) Extracellular matrix of glioblastoma inhibits polarization and transmigration of T cells: a role of tenascin-C in immune suppression. J. Immunol. 185:1450-1459..
- Lin YP, Cheng YJ, Huang JY, Lin HC, and Yang BC (2010) Zap70 controls the interaction of talin with integrin to regulate the chemotactic directionality of T cell migration. Mol Immunol. 47(11-12):2022-9.
- Su CC, Lin YP, Cheng YJ, Huang JY, Chuang WJ, Shan YS, Yang BC (2007) Phosphatidylinositol 3-kinase/akt activation by integrin-tumor matrix interaction suppresses fas-mediated apoptosis in T cells.
 J Immunol. 179:4589-4597.

