



INSTITUTE FOR CELLULAR ENGINEERING

Targeting drug-resistant tumor regions using engineered bacteria

IGERT Associate Miaomin Zhang

PI: Prof. Neil Forbes (UMass Chemical Engineering)



Tiled reconstructions of histological sections of Brown-Hopps stained subcutaneous MCaIV tumors in a C3H mouse administered *S. typhimurium*. Red – bacterial colonies; yellow – tumor tissue sparsely populated with bacteria; green – functional vasculature within the tumor.

The microenvironment inside solid tumors is highly heterogeneous. Current therapies do not actively transport and are weak in tumor penetration. In our lab, we are interested in engineering bacterium *Salmonella typhimurium* to create a novel drug delivery system. Previously in tumor cylindroids, we have shown that the aspartate receptor initiates bacterial migration toward tumors, the serine receptor controls penetration, and the ribose/galactose receptor directs *Salmonella* into necrosis. Work has also been initiated to study the spatio-temporal characteristics of the bacterial distribution throughout tumors in mice. My work is to develop these two aspects of research and bring them together.

The first task I need to accomplish is knocking out the gene for the ribose/galactose receptor. We hypothesize that this causes *S. typhimurium* to accumulate in the quiescent regions, which is not as deep as the necrotic regions in tumors but notoriously therapeutic-resistant. The engineered bacteria will then be intravenously injected into tumor-bearing mice. Tumor samples will be collected from euthanized mice and analyzed by ways of statistical/mathematical modeling.