Real-time in vivo cancer diagnosis with a Microelectromechanical Systems (MEMS) based handheld Dual-Axes Confocal Microscope

Biomedical research truly needs new advances in imaging. Existing modalities of *in vivo* imaging, such as magnetic resonance imaging (MRI) or ultrasound, lack the spatiotemporal resolution required to image the fundamental building block of living tissue, namely the cells. By contrast, existing high-resolution techniques for imaging cells and their sub-cellular features are technologies that are best suited for *in vitro* experiments in tissue slices. Yet, the ability to make direct connections between human pathological symptoms/behavior and the underlying cells and molecules responsible for such behavior requires *in vivo* techniques that can image cellular constituents. My research aim is to develop a novel high-resolution optical endoscope (1 to 10 mm diameter) to satisfy unmet needs in the clinical environment. These differ from medical endoscopes, which are generally larger and designed to image macroscopic abnormalities. Most importantly, this novel optical endoscopic imaging might suggest new approaches to drug/disease monitoring, diagnosis, and treatment.

This talk will be focused on the development a novel imaging modality called dual-axes confocal (DAC) fluorescence microscope based on microelectromechanical systems (MEMS) technology. The DAC microscope offers several advantages over the traditional single-axis confocal (SAC) architecture such as simplicity in miniaturization from deploying low numerical aperture (NA) lenses and aberration-free beam scanning from post-objective scanning configuration. The other important advantage is the ability to achieve a much superior optical sectioning compared to the SAC design.

Recently, there is lots of interest in the development of RNA interference. This is due to the fact that it offers the potential of a novel therapeutic approach for treating skin disorders and other diseases. The ability to design, screen and identify potent, selective and stable small interfering RNAs (siRNAs) is now relatively straightforward. Unfortunately, methodologies to deliver these potential therapeutics to appropriate cells (including skin cells) has not kept pace. The long-term goal of this project is to develop effective and efficient siRNA skin delivery technologies, facilitating translation of siRNA therapeutics to the clinic.

The development and application of the DAC imaging system allows noninvasive monitoring of the effectiveness of functional siRNA in individual cells and cancer diagnosis in real time by visualization of reporter gene expression in transgenic murine skin and monitoring morphological changes of normal tissues into diseased tissues. Imaging demonstrations of the DAC microscope will be on 1) *in vivo* skin imaging of functional siRNAs on mouse model systems and 2) *ex vivo* human tissues (skin, colon, esophagus, and stomach).