

**UNIVERSITY OF TOLEDO HEALTH SCIENCE CAMPUS  
2008 MEDICAL STUDENT SUMMER RESEARCH AWARD APPLICATION**

1. **Faculty Name:** Akira Takashima, M.D., Ph.D.
2. **Academic Rank:** Professor and Chairman
3. **Department:** Medical Microbiology & Immunology
5. **Name(s), Academic Rank, and Department(s) of any Co-Investigators:** N/A
6. **Project Title:** Intravital Imaging of Langerhans Cell Behavior
7. **Brief Summary/Description of Project: (Limit this section to one page. Include a well-defined Specific Aim for the student's project and related methodology. DO NOT append a copy of your grant application.)**

Langerhans cells (LCs) are skin-resident immature dendritic cells (DCs) that perform two key surveillance tasks (antigen sampling and detection of danger signals) at the environmental interface. Our objective is to define behavioral mechanisms by which LCs achieve these tasks in their natural habitat (i.e., skin). For this purpose, we have recently developed a novel imaging system to acquire 4D images of LCs in living mice. Briefly, LCs are visualized in the skin of I-A $\beta$ -EGFP knock-in mice in which enhanced green fluorescent protein (EGFP) is expressed only by DCs. We will record 4-dimensional images of EGFP<sup>+</sup> LCs every 2 min for 4 h by "time-lapse" multi-photon laser scanning microscopy in anesthetized I-A $\beta$ -EGFP knock-in mice to measure spatiotemporal kinetics of individual motile activities of EGFP<sup>+</sup> LCs. In the steady state, LCs exhibit dSEARCH motion (characterized by extension and retraction of dendrites), amoeba-like lateral migration, vertical migration, and LC-LC contact formation. A key question now concerns the potential impact of environmental hazards on dynamic behaviors of LCs. In this regard, ultraviolet B (UVB) radiation is known to promote skin cancer development by suppressing the immuno-surveillance function of LCs, although underlying mechanisms remain to be determined. Thus, we propose to test the hypothesis that UVB radiation alters the in situ behaviors of LCs in the skin. The main objects of this short-term project include: a) to optimize the UVB irradiation protocol, b) to record 4D images of EGFP<sup>+</sup> LCs after UVB exposure, and c) to define behavioral responses of LCs to UVB radiation in a quantitative manner. Our study should provide important insights into the behavioral biology of LCs and the pathophysiology of UVB-induced skin cancer development.

8. **Describe Student's Role and Responsibilities.**

The student will record 4-dimensional images of EGFP<sup>+</sup> Langerhans cells in anesthetized mice following local ultraviolet B exposure. The student also will be responsible for processing the datasets to measure behavioral responses of Langerhans cells in a quantitative manner by using advanced programs for image analyses.

9. **Special Qualifications Required (NAME OF STUDENT, IF IDENTIFIED).**

- a) Full commitment to the research opportunity
- b) Basic knowledge in Immuno-biology

c) Willingness to work on a challenging project