2026 Student Research Fellowship Program

Project title: Role of FAK in Human Urothelial Cell Migration and Proliferation

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Location: RGE 100

PROJECT DESCRIPTION

Abstract of Project.

Ulcerative cystitis is a debilitating condition characterized by ulcerative lesions within the bladder lining, including Hunner-type interstitial cystitis (IC) and hemorrhagic chemical (cyclophosphamide, ifosfamide, or ketamine–induced) or radiation cystitis. Damage to the superficial urothelial layer exposes underlying tissues to urine, solutes, and toxins, triggering inflammation and hematuria. This results in significant pain and a spectrum of lower urinary tract symptoms (LUTS)—including frequency, urgency, incontinence, dysuria, suprapubic pain, hematuria, and incomplete bladder emptying—that severely impair quality of life. Although the incidence of ulcerative cystitis continues to rise, effective treatments remain limited.

Focal Adhesion Kinase (FAK) is a protein tyrosine kinase that functions as a scaffold linking the cytoskeleton to the extracellular matrix through focal adhesions. We have demonstrated that a newly developed FAK activator, M64HCl, accelerates mucosal healing in a rat model of acetic acid–induced intestinal injury (*BMC Gastroenterol.* 2025, 25:347). We hypothesize that M64HCl can be repurposed to address the critical unmet need in ulcerative cystitis by promoting urothelial repair through FAK activation. To test this hypothesis, we conducted a pilot in vivo study showing that subcutaneous administration of M64HCl before intraperitoneal cyclophosphamide (CYP) significantly reduced hemorrhage and urothelial denudation four days after CYP administration in mice. To translate these findings toward clinical application, our next step is to determine whether M64HCl increases p-FAK levels and enhances adhesion, migration, and proliferation in primary human bladder urothelial cells, as well as to elucidate its underlying molecular mechanisms. This will be the focus of the summer student fellow's project. The student will culture primary human bladder urothelial cells, measure FAK and p-FAK expression, and assess cell adhesion, migration, and proliferation following FAK inhibition/gene knockdown or activation/gene overexpression. Additionally, gene expression profiles of focal adhesion and cytoskeletal regulators will be analyzed, and phosphoproteomic profiling will be performed to identify mechanistic pathways. Key target molecules will be further validated through gain- and loss-of-function experiments.

Significance.

Despite the increasing incidence of ulcerative cystitis, treatment options remain inadequate. Common therapies - such as systemic amitriptyline, prednisolone, and cyclosporine A, or intravesical agents like dimethyl sulfoxide, hyaluronic acid, and lidocaine - are used particularly for Hunner-type IC. However, these treatments are primarily symptomatic, often lack robust evidence, show limited efficacy, and may cause significant side effects. In severe or refractory cases, cystectomy with urinary diversion is considered a last-resort option. Many patients report profound dissatisfaction with current medical care. Our preclinical pilot results are highly encouraging, demonstrating that the novel FAK activator M64HCl can alleviate CYP-induced ulcerative cystitis in mice. The long-term objective is to translate these findings into a first-in-human clinical trial. Rigorous evaluation of M64HCl's effects and mechanisms in human bladder urothelial cells is therefore a critical next step. This work will significantly accelerate translational progress and has the potential to provide a much-needed therapeutic option for patients with ulcerative cystitis.

Research methods that will be learned by the student.

- Cell culture
- Adhesion, migration, and proliferation assays
- RNA isolation, cDNA synthesis, PCR
- Protein quantification
- Western blotting
- Statistical analysis

Proposed methods of data analysis.

Statistical analyses will be performed using GraphPad Prism (GraphPad Software, La Jolla, CA). Normally distributed data will be presented as mean ± standard deviation (SD). Comparisons among multiple groups will be analyzed using ANOVA followed by the Tukey-Kramer post hoc test. Comparisons between two groups will be conducted using an unpaired, two-tailed t-test. P-values < 0.05 will be considered statistically significant.

How will the anticipated findings contribute to the success of the overall research?

If successful, this will accelerate the translation of a promising preclinical result into a future clinical trial. This treatment represents a fundamentally novel therapeutic strategy compared to existing approaches. In addition, the data generated could serve as important preliminary evidence to support future grant applications.

STUDENT FELLOW TRAINING/MENTORING PLAN

The student will receive daily guidance from Dr. Liu and members of the Basson - Liu Laboratory. They will participate in weekly laboratory meetings focused on experimental design and data analysis and will present their progress regularly. Depending on the student's interests, opportunities may be available to engage in additional ongoing projects, including rodent studies. The student will also participate in seminars offered by the Department, College, and University. It is anticipated that the student will prepare a poster or oral presentation for Student Research Day and that the data generated will contribute to a future publication on which the student will be included as a co-author.