Faculty Member Contact Information

Name	Dr. Maria Kontoyiani
Contact Info	
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Campus Box	2000
Department	Pharmaceutical Sciences

1 Funded, 1 Unfunded URCA Assistant

	This position is **ONLY** open to students who have declared a major in this discipline.	
	This project deals with social justice issues.	
	This project deals with sustainability (green) issues.	
	This project deals with human health and wellness issues.	
	This project deals with community outreach.	
X	This mentor's project is interdisciplinary in nature.	

Are you willing to work with students from outside of your discipline? If yes, which other disciplines?

- Yes, my project is truly interdisciplinary, please also mark me as interested in taking students from these areas: Chemistry, Computer Science, Biochemistry

How many hours per week will your student(s) be required to work in this position? (Minimum is 6 hours per week; typical is 9)

- 9-10

Will it be possible for your student(s) to earn course credit?

- None

Location of research/creative activities:

- Science East, Suite 3280

Brief description of the nature of the research/creative activity?

The somatostatin receptors (SSTs) are divided into two subfamilies: 1 (SST2, SST3, SST5) and 2 (SST1, SST4) based on sequence homology, ligand binding profiles, and phylogenesis. Our lab developed a structure-based drug design (SBDD) strategy for SST4 agonists, employing computational methods towards an Alzheimer's therapeutic. This work has been a collaborative effort with SIUE chemistry and pharmacology labs, and resulted in a patent and multiple publications.

In an effort to explore the basis for the structural diversity of ligands reported to bind to different SST subtypes, we are currently developing a classification model correlating physicochemical properties of the small binders with characteristics of the binding pocket of each SST. However, no machine learning is 100% predictive, thus our next step will be to try to understand why the model fails to wrongly predict the respective SST receptor for certain small molecules. Towards that end we plan to perform docking of these inaccurately predicted structures, meaning we will computationally place them into their respective macromolecules to identify which characteristics of the binding pockets are failing. Analysis of the classification model and docking results will be the responsibilities of the prospective URCA student. Another aspect of this research is to explore whether different configurations of the SST4 subtype result in more accurate docking placements. Thus far, we have employed rigid receptors for the SBDD methodology. However, we wish to understand why in certain cases we were unable to observe consistency in binding. The student will set up some molecular dynamics (MD) simulations, by (1) refining the SST4 macromolecule in reference to bond lengths and angles, and overall packing; (2) embedding it into a lipid bilayer using CHARMM-GUI; (3) preparing the input files for MD, and (4) submitting the MD runs to the cluster.

Brief description of student responsibilities?

(1) Evaluate classification models; (2) perform docking of the compounds which failed to be accurately predicted by the classification model, using a software in the lab; (3) understand what drives diversity, meaning why certain small molecules bind to a specific SST subtype and not another; (4) prepare SST4 structures with appropriate bonds, charges and correct crystal packing, using an existing software; (5) embed the macromolecules into a bilayer using CHARMM-GUI; 3) learn how to edit input files which are prepared by the CHARMM-GUI; (6) run molecular dynamics (MD) simulations. If MD runs finish in time, a visualizer of the will be employed to explore SST4 configurations.

URCA Assistant positions are designed to provide students with *research or creative activities* experience. As such, there should be measurable, appropriate outcome goals. What exactly should your student(s) have learned by the end of this experience?

Most importantly, they will develop critical thinking. They will be able to look at results and realize whether there are discrepancies, whether the findings of the methodologies support or invalidate our initial hypotheses, and how to best proceed or interpret observations. Technically, they will also: 1. learn how to refine a crystal structure; 2. how to run machine learning; 3. learn some unix; 4. learn to use visual molecular dynamics and NAMD. Finally, they will be co-authors in one or two publications.

Requirements of Students

If the position(s) require students to be available at certain times each week (as opposed to them being able to set their own hours) please indicate all required days and times:

- N/A

If the location of the research/creative activities involves off campus work, must students provide their own transportation?

- N/A

Must students have taken any prerequisite classes? Please list classes and preferred grades:

- N/A

Other requirements or notes to applicants:

- None