Dr. Jason Choi

PROJECT SUMMARY/ABSTRACT

Laminopathies are a diverse group of diseases arising from mutations in LMNA that encodes the A-type lamins A and C. Mutations in LMNA lead to tissue-selective diseases, the most common of which is dilated cardiomyopathy (LMNA cardiomyopathy). There is a dearth of insights into mechanisms by which mutations in LMNA cause dilated cardiomyopathy. Due to this fact, there is no specific therapeutic intervention that improves cardiac performance or prevents heart muscle deterioration. My overall goal is to reveal mechanistic insights into LMNA cardiomyopathy and, based on the new knowledge, develop mechanism-based therapeutic strategies. To this end, I have already made significant inroads into this goal, by identifying Dusp4 as a mediator of LMNA cardiomyopathy. One of the main objectives of this project is to extend on my findings and cover gaps in our current understanding of the Dusp4-mediated pathogenic mechanisms that drive LMNA cardiomyopathy. The proposed aims will take a multidisciplinary approach, spanning molecular and biochemical analyses to in vivo mouse genetics and live animal studies, with the ultimate goal of rapidly translating the gained knowledge into new clinical practice.

Another main objective of this project is to continue my development as an independent scientist capable of conducting high quality multidisciplinary research. This entails two major areas of training: 1) additional scientific training through my mentor, co-mentors, didactic courses available at Columbia University, and attending national meetings and 2) career developmental training through grant writing workshops, courses in responsible conduct of research, conflicts of interest, manuscript preparation and presentation workshops, and lab/budget management. The collective training I will receive will help me attain my goal of finding a faculty position and establishing my own independent research program by successfully competing for RO1 funding.

My short-term goals are to:

1. Identify pathogenic mechanisms mediated by Dusp4 in LMNA cardiomyopathy.
2. Continue my scientific and career development through my mentor, co-mentors, and didactic courses.
3. Advance my career by securing an independent faculty position and expanding my network of colleagues.

My long-term goals are to:

1. Continue my scientific work, devise and perform preclinical studies based on new results obtained.
2. Attain RO1 funding, establish independent research program, and continue career development training.
3. Translate our findings into new therapies, train future mentees, and maintain successful research program.
