**Exploring the function of the intrinsically disordered region (IDR) of the cell junction-cytoskeletal crosslinker Canoe.**

Godwin Agbeka1,2, Yufei Xiao2, Noah Gurley2, Avery Mathias2, Corbin Jensen2, and Mark Peifer2,3,4\*

1. Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; 2. Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; 3. Curriculum in Genetics and Molecular Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; 4. Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

**Abstract**

During embryonic development, epithelial cells change shape and move to form crucial tissues and organs. This is achieved by linking these cells to each other via cell-cell adherens junctions (AJs) and connecting these junctions to the cytoskeleton. It is now known that the formation and function of AJs is not simple but involves a complex interplay of molecules linking junctions to the cytoskeleton. One such molecule is Canoe - the *Drosophila* counterpart of human Afadin - which plays a central role by strengthening junction-cytoskeletal connections to maintain epithelial cell integrity and prevent tissue disruption during cell movement and apical constriction. We suspect Canoe acts within a very large adhesion complex, with hundreds of proteins linked by multivalent interactions. Canoe is a multidomain protein and our lab has characterized the functions of multiple Canoe domains. We are now focused on the function of the less conserved intrinsically disordered region (IDR) of Canoe (Cno)/Afadin. Using mutants deleting the IDR (*cno∆IDR*), we have found that this region of the protein is important for protein function, and homozygous mutants die as embryos with strong defects in embryonic morphogenesis. However, to our surprise, when we divided the IDR into three regions and individually deleted each region (*cno∆N, cno∆H, cno∆C*), each of the mutants is homozygous viable. We thus wondered if animals heterozygous for *cno∆IDR* and each of the smaller IDR deletions would be viable, and if embryos with this genotype would have defects in embryonic morphogenesis. My data suggest that *cno∆N* and *cno∆C* do not retain fully wildtype function, as we recover far few progeny of those alleles over *cno∆IDR* than expected-- *cno∆C* is even less functional in this assay than *cno∆N.* I examined the embryonic phenotypes of *cno∆IDR/cno∆N,* using a wildtype *cno* gene as a control through immunostaining and confocal microscopy or larval cuticles. Together, my data suggest that subregions of the IDR are not essential but contribute to full protein function.