Biochemical Approaches to Characterize the Molecular Basis of Abnormal Cell Signaling Function Involving Ras-Related Proteins

Ras proteins are often mutated in many human cancers, making them excellent protein models to probe structure-function relationships of cell-signaling processes mediating cell transformation. Target-based approaches to avert Ras-related signal transduction activity leading to diseased states such as cancer should be enhanced by a better understanding of the correlates among the structural biology of protein-protein interactions, as well as, protein function. Cell division cycle 42 (Cdc42) and Ras homology enriched in brain (Rheb) are members of the Ras family of proteins, which were among the first human oncogenic proteins to be identified, and are the model Ras protein systems being studied by this laboratory. Mutations or abnormal expression of Ras proteins play a significant role in events leading to cellular proliferation, inhibition of cell death, and tumor development. As such, novel approaches are needed to fill the gaps in our understanding of important molecular details of mutant Ras protein interactions that may highlight new ways to control potentially aberrant Ras-related cell-signaling activity.

Long-term goals of this research are to understand key factors, using biophysical and biochemical techniques and approaches, that underlie the molecular basis of aberrant signaling behavior involving Ras-related proteins that lead to cell transformation, proliferation, and metastasis. The central hypothesis of our research objective is that there are unique structural and dynamic features of Ras proteins that can be exploited to modulate protein interactions and influence abnormal cell signaling activity. Once key molecular features of Ras protein constructs with altered protein interactions are known, new avenues in the development of strategies to target the inhibition of Ras-protein interactions with oncogenic potential may be approached. Recent results from the laboratory suggest that, in addition to strategies to block Ras-protein interactions, strategies to restrict the conformational flexibility of important binding regions of Ras-related proteins leading to the inhibition of effector interactions that facilitate aberrant signaling activity may also have therapeutic potential.

Lunch provided for students with the seminar speaker from 12:00 – 1:15 pm in Laney Hall Rm 105.
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