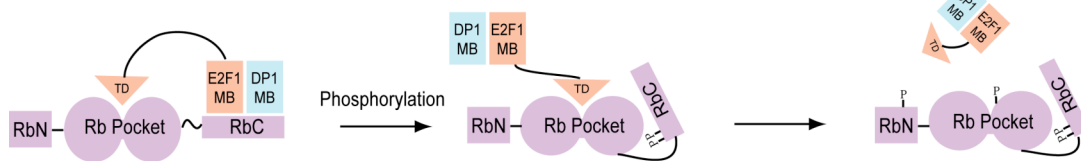


Our research focuses on understanding the biochemical mechanisms that regulate cell growth and division and how defects in these mechanisms result in diseases such as cancer. The cell cycle is coordinated by a shifting network of protein-protein interactions. We develop and use a number of structural and biophysical techniques, particularly x-ray crystallography and nuclear magnetic resonance (NMR), to characterize these interactions at atomic resolution and use molecular biology and biochemical methods to understand their relevance in the cell.

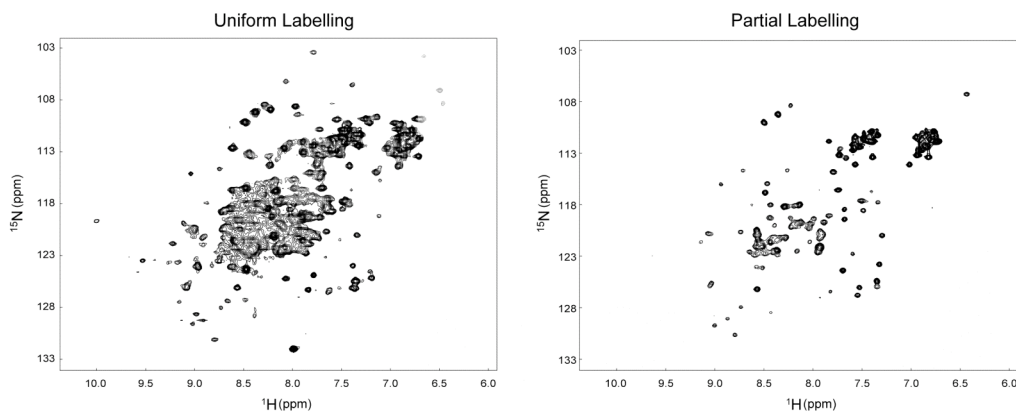
We currently study two protein families that control the G1 to S phase transition of the eukaryotic cell cycle and potentially play a critical role in tumorigenesis. Members of the E2F family of transcription factors activate genes required for DNA synthesis and other processes towards cell division. The retinoblastoma (Rb) and related “pocket proteins” bind and inhibit E2F until the cell is ready to begin S phase. At this point, Rb is phosphorylated by cyclin-dependent kinase (Cdk)-Cyclin complexes and E2F is activated through its release. While this simple model for the biological role of Rb as a growth regulator is clear, the biochemical mechanisms underlying Rb function remain unexplained. Our goal is to understand in molecular detail the interactions of Rb with E2F and other regulatory proteins and how these interactions are affected by phosphorylation.

Model for phosphorylation induced dissociation of the Rb-E2F-DP complex



While NMR is particularly useful for studying protein conformational changes and binding interactions, current methodology limits experimentation on proteins with molecular weight greater than ~30 kDa. A second focus in the laboratory is to develop new methodologies, particularly isotope labeling strategies, to enable NMR studies of relatively large cell cycle related proteins. Selective amino acid type labeling will be combined with cell free protein expression methods to generate novel samples that facilitate data analysis by reducing spectral complexity.

H-N correlation NMR spectra of a ~30kDa E2F1-DP1 complex



If you are interested in conducting postdoctoral, graduate, or undergraduate research in our laboratory or would like more information, please contact Professor Rubin at srubin@ucsc.edu.

Selected Publications

Rubin, S.M., Gall, A.-L., Zheng, N., & Pavletich, N.P. Structure of the Rb C-terminal Domain Bound to an E2F1-DP1 Heterodimer: A Mechanism for Phosphorylation-Induced E2F Release. *Cell*, **2005**, **123**(6), 1093-1106.

Rubin, S.M., Pelton, J.G., Yokota, H., Kim, R., Wemmer, D. E. Solution Structure of a Putative Ribosome Binding Protein from *Mycoplasma pneumonia* and Comparison to a Distant Homolog. *J. Struct. Func. Gen.*, **2003**, **4** (4), 235-243.

Rubin, S.M., Lee, S.-Y., Ruiz, E.J., Pines, A., & Wemmer, D. E. Detection and Characterization of Xenon Binding Sites in Proteins by ^{129}Xe NMR Spectroscopy. *J. Mol. Bio.*, **2002**, **322**, 425-440.

Rubin, S. M., Spence, M. M., Dimitrov, I. E., Ruiz, E. J., Pines, A. & Wemmer, D. E. Detection of a Conformational Change in Maltose Binding Protein by ^{129}Xe NMR Spectroscopy. *J. Am. Chem. Soc.*, **2001**, **123**(35), 8616-8617.