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Education:

- A.B., 1976, University of California, Berkeley
- M.A., 1978, Columbia University
- Ph.D., 1982, Columbia University
- Postdoc., 1982-1986, The Rockefeller University
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Research Interest:

- **Cancer Biology**
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Our lab has two major research focuses. The first is the promotion of cancer cell survival by the generation of the oncometabolite phosphatidic acid (PA). PA is generated by several different mechanisms including - de novo membrane phospholipid biosynthesis, diacylglycerol kinase (DGK), and phospholipase D (PLD). PA is critical for the activation of mTOR – the mammalian target of rapamycin – a critical integrator of both growth factor and nutrient signals. Since PA is the product of glycolysis and fatty acid synthesis, it is proposed that PA requirement of mTOR represents a key nutrient input to mTOR indicating that there is sufficient glucose and lipids available for a dividing cell to double its mass and form two daughter cells. The generation of PA by DGK and PLD likely evolved as a means to regulate PA levels and mTOR via growth factor signals. In this regard, it is significant that PLD activity is elevated in virtually all cancer cells where it has been investigated. The second major focus of the lab is the metabolic control of cell cycle progression. A major hallmark of cancer is the dysregulation of G_1 cell cycle checkpoints. We have identified several late G
1
checkpoints that are sensitive to the presence of – essential amino acids, the “conditionally” essential amino acid glutamine, lipids and another mediated by mTOR. Importantly, KRas-driven cancer cells override the glutamine checkpoint and arrest in S-phase rather than G
1
when deprived of glutamine. The S-phase arrest makes KRas-driven cancers (about 30% of human cancer) sensitive to S-phase-specific cytoxic drugs, including rapamycin. In this way, we are exploiting metabolic vulnerabilities of cancer cells to develop strategies to target specifically the cancer cells. These two major focuses of the lab – dysregulated cell cycle progression and PA metabolism – intersect at mTOR, which has been referred to as the most dysregulated signaling node in human cancer.

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Selected Publications (from 120):

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