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## MAJOR RESEARCH INTERESTS

Research in my laboratory concentrates on signal transduction in cells, with a focus on two disparate pathways: Wnt, and circadian rhythms. In both cases, we study the protein kinases and phosphatases that control the activity of these pathways, working to understand the fundamental mechanisms of control. We use biochemical, cell-based and animal models to understand how these mechanisms impact proliferation, differentiation, and timing.

Current projects include:

1. Understanding how Wnt ligand regulates the activity of GSK3
2. The study of phosphorylation-regulated degradation of circadian regulators PER1 and PER2, in collaboration with several labs in the USA.
3. Studying Wnt biogenesis and its role in cancer, using both knockout mice and small molecule inhibitors.

## RECENT PUBLICATIONS

1. Eide EJ, Woolf MF, Kang H, P Woolf, F Camacho, EL Vielhaber, A Giovanni, **DM Virshup** (2005) Control of mammalian circadian rhythm by CKIε-regulated proteasome-mediated PER2 degradation. *Molecular and Cellular Biology*, 25:2795-807.
2. Beth A. Firulli, D Krawchuk, VE Centonze, **David M. Virshup**, SJ. Conway, Peter Cserjesi, Ed Laufer and Anthony B. Firulli. (2005) Altered Twist1 and Hand2 dimerization is associated with Saethre-Chotzen syndrome and limb abnormalities. *Nature Genetics*, 37:373-381.
3. Swiatek, W., Kang, H., Garcia, B. A., Shabanowitz, J., Coombs, G. S., Hunt, D. F. and **Virshup, D. M.** (2006) Negative regulation of LRP6 function by casein kinase I epsilon phosphorylation *Journal of Biological Chemistry* 281, 12233-12241]
4. Gallego M, Eide EJ, Woolf M, **Virshup DM**, Forger D. (2006) An opposite role for tau in circadian rhythms revealed by mathematical modeling. *Proceedings of the National Academy of Science (USA)* 103:10618-23
5. Gallego M, Kang H, **Virshup DM**. Protein Phosphatase 1 Regulates The Stability Of The Circadian Protein Per2. (2006) *Biochemical Journal*, 399:169-75.
6. Klimowski L, Garcia B, Shabanowitz J, Hunt D, **Virshup DM**. Site-specific CKIε-dependent phosphorylation of Dishevelled modulates β-catenin signaling. (2006) *FEBS J*. 273:4594-602.
7. Margolis SS, Perry JA, Forester CM, Nutt LK, Guo Y, Jardim MJ, Thomenius MJ, Freel CD, Darbandi R, Ahn JH, Arroyo JD, Wang XF, Shenolikar S, Nairn AC, Dunphy, WG, Hahn WC, **Virshup DM**, Kornbluth S. (2006) Role for the PP2A/B56delta phosphatase in regulating 14-3-3 release from Cdc25 to control mitosis. *Cell*. 2006 127:759-73.
8. Wen Luo, Annita Peterson, Benjamin A. Garcia, Gary Coombs, Bente Kofahl, Reinhart Heinrich, Jeffrey Shabanowitz, Donald F. Hunt, H. Joseph Yost, and **David M. Virshup**. (2007) Protein phosphatase 1 regulates assembly and function of the β-catenin degradation complex. *EMBO Journal*. 26:1511-21.
9. I-Chun Tsai, Jeffrey Amack, Zhong-Hua Gao, Vimla Band, H. Joseph Yost, **David M. Virshup**. (2007). A Wnt-CKIε-Rap1 Pathway Regulates Gastrulation by Modulating SIPA1L1, a Rap GTPase Activating Protein. *Developmental Cell*, 12:335-47