

# Cancer Cell Signaling

## Principal investigator(s) and affiliation(s), contact information

Jukka Westermarck, MD, PhD, Professor  
Centre for Biotechnology, University of Turku and Åbo Akademi University  
Turku, Finland  
E-mail: jukwes@utu.fi  
Phone: 333 8621 Mobile: 040 7423007

## Members of the research group

### Doctoral candidates:

Amanpreet Kaur, MSc  
Eleonora Mäkelä, MSc  
Otto Kauko, MD, MSc  
Xi Qiao, MSc

### Post-docs:

Anna Lipsanen, PhD  
Anni Laine, PhD  
Christian Rupp, Ph  
Karolina Pavic, PhD  
Oxana Denisova, PhD

### Technicians:

Taina Kalevo-Mattil  
Johanna Jukkala, MSc (50 %)

### Laboratory Manager:

Tiina Arsiola, PhD



## Description of the scientific aims

Protein phosphatase 2A (PP2A) is a trimeric protein phosphatase complex consisting of catalytic C-subunit (PP2Ac), scaffolding A-subunit (PR65) and various regulatory B-subunits. PP2A functions as a tumor suppressor by dephosphorylating several critical cancer drivers. The focus of our laboratory is to understand role and regulation of PP2A in human cancers and especially function of PP2A inhibitor proteins as human oncoproteins. Our recent results suggest that a potential biological outcome of aberrant PP2A signaling in cancer is conferring drug resistance. Based both on these results, and on wide-spectrum role of PP2A on cellular signaling, we hypothesize that re-activation of PP2A, via targeting of its endogenous inhibitory proteins, could be used as a general strategy for multi-target inhibition of chemoresistance in common human cancer types.

## Selected publications 2010-

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2. Myant K, Qiao X, Halonen T, Come C, Laine A, Janghorban M, Partanen JI, John Cassidy, Ogg E-L, Cammareri P, Laiterä T, Okkeri J, Klefström J, Sears RC, Sansom OJ\*, Westermarck J\*. Serine 62 phosphorylated MYC associates with nuclear lamins and its regulation by CIP2A is essential for regenerative proliferation. *Cell Rep*, 12(6):1019-31, 2015.
3. Ventelä S, Sittig E, Mannermaa L, Mäkelä J-A, Kulmala J, Löyttyniemi E, Strauss L, Cárpen O, Toppari J, Grénman R and Westermarck J; CIP2A is an Oct4 target gene involved in head and neck squamous cell cancer oncogenicity and radioresistance. *Oncotarget*, 6(1):144-58, 2015.
4. Khanna A, Kauko O, Böckelman C, Laine A, Schreck I, Partanen JI, Szwadja A, Bormann S, Bilgen T, Helenius M, Pokharel YR, Pimanda J, Russel MR, Haglund C, Cole KA, Klefström J, Aittokallio T, Weiss C, Ristimäki A, Visakorpi T, Westermarck J. Chk1 targeting reactivates PP2A tumor suppressor activity in cancer cells. *Cancer Res*, 73(22):6757-69, 2013.
5. Laine A, Sihto H, Come C, Rosenfeldt MT, Zwolinska A, Niemelä M, Khanna A, Chan EK, Kähäri V-M, Kellokumpu-Lehtinen P-L, Sansom OJ, Evan GI, Junttila MR, Ryan KM, Marine J-C, Joensuu H, Westermarck J. Senescence sensitivity of breast cancer cells is defined by positive feedback loop between CIP2A and E2F1. *Cancer Discov*, 3(2):182-197, 2013.