

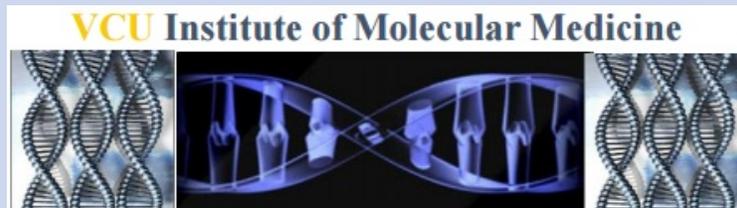

**VCU**

VIRGINIA COMMONWEALTH UNIVERSITY

# Institute of Molecular Medicine

## VCU Institute of Molecular Medicine (VIMM) NEWS & VIEWS

The VIMM, established in 2008 by Paul B. Fisher, M.Ph., Ph.D., the Founding Director, is comprised of outstanding scientists/clinicians from VCU School of Medicine focusing on important medical-related research in cancer, neurodegeneration and infectious diseases. The purpose of this NEWS & VIEWS is to highlight the exciting research being performed by the VIMM members.



### A New Look at the Roles of PLK1 in Prostate Cancer

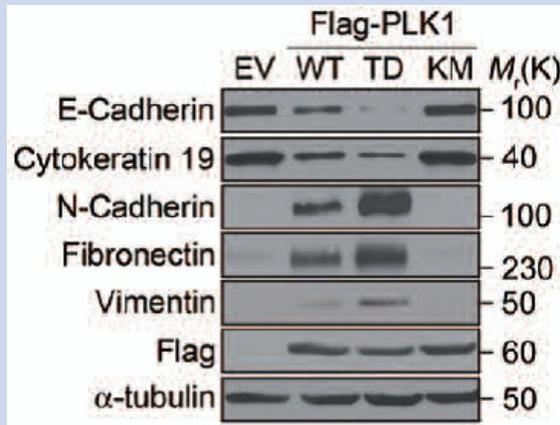
- Polo-like kinase 1 (PLK1) is a serine/threonine kinase that plays key roles in the control of the cell cycle.
- An increased level of PLK1 has been implicated in the development of various cancers, including prostate cancer.
- The current knowledge in the field is that PLK1 controls cancer development mainly through its established regulation of mitosis and cell division.
- This study discovered that PLK1 plays a causal role in epithelial-to-mesenchymal transition (EMT) and metastasis and that PLK1 is a potent activator of MAPK signaling.
- This new insight could not only advance the understanding of the cancer-promoting functions of PLK1 and the molecular basis of prostate cancer development and metastasis, but also facilitate optimization of treatments targeting PLK1 signaling to significantly enhance the efficacy of anticancer therapies.

### New Insights into the Oncogenic Functions of Polo-Like Kinase 1 in Prostate Cancer Development

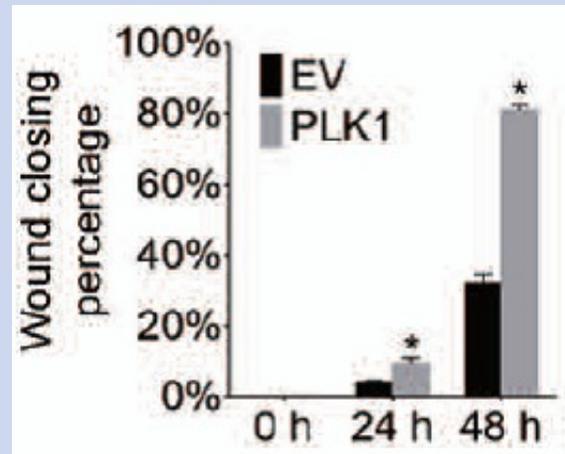
Mammalian polo-like kinase 1 (PLK1) is a serine/threonine kinase that plays key roles in the regulation of the cell cycle. PLK1 is overexpressed in a variety of human tumors and its expression level often correlates with increased cellular proliferation, enhanced metastatic potential, and poor prognosis in cancer patients. This study challenged the current dogma in the field emphasizing the mitotic activity of PLK1 as a primary mechanism of its oncogenic function. Instead, it was demonstrated that PLK1 drives cell cycle independent migration of

normal prostate epithelial cells and also prostate cancer cells. This work shows, for the first time, that PLK1 stimulates the motility and invasiveness of normal prostate epithelial cells and prostate cancer cells by inducing epithelial-to-mesenchymal transition (EMT). This previously unanticipated pro-migratory activity of PLK1 is driven by its direct activation of a key oncogene, CRAF. This results in enhanced signaling through the mitogen activated protein kinase (MAPK) signaling pathway. The functional outcome of such MAPK activation is induction of EMT and stimulation of cancer cell motility. The novel findings that PLK1 plays a causal role in EMT and metastasis, and that PLK1 is a potent activator of MAPK signaling have advanced our understanding of the cancer-promoting functions of PLK1 and the molecular basis of prostate cancer development and metastasis. This knowledge could facilitate optimization of treatments targeting PLK1 signaling to significantly enhance the efficacy of anticancer therapies. This study was published in the journal *eLIFE* on March 22, 2016\*.

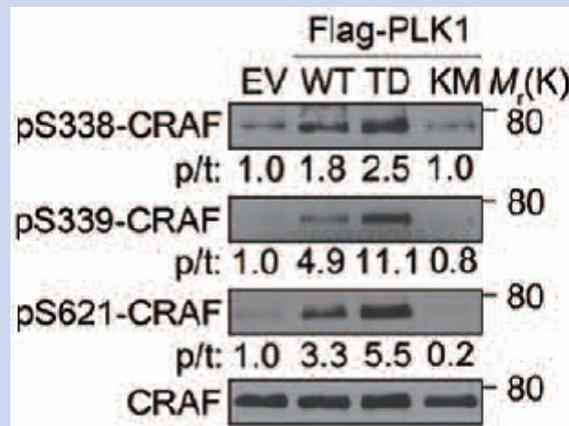
**A**

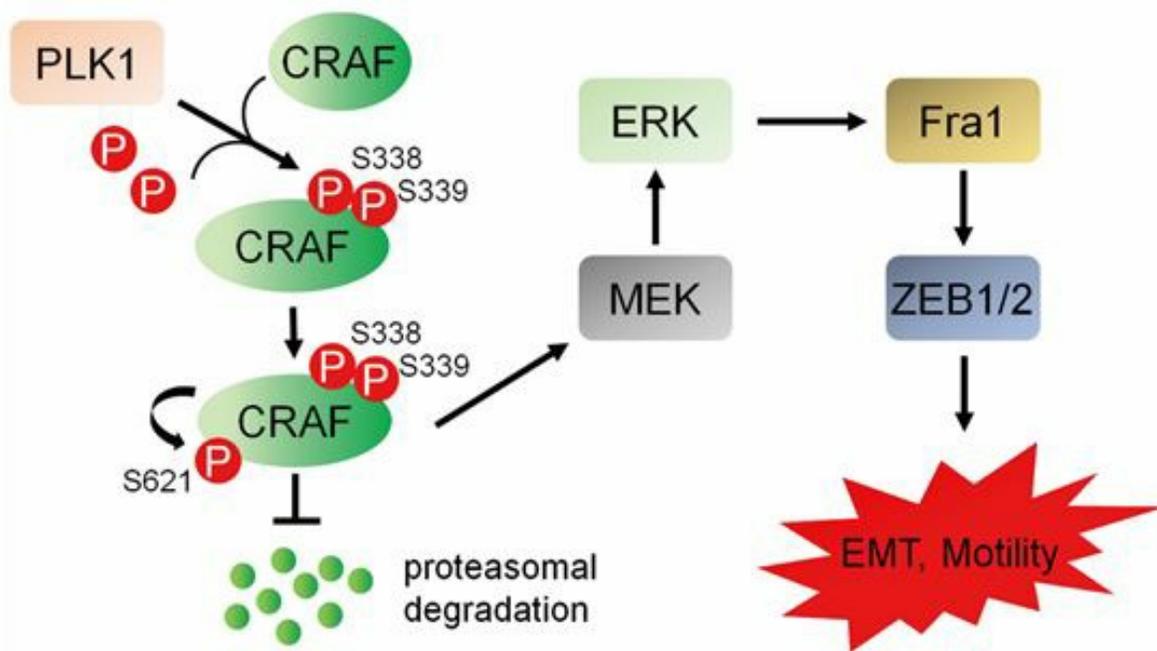


**B**



**C**





**Figure legend.** PLK1 mediates induction of EMT and cell motility (A) RWPE-1 cells were infected with lentivirus expressing wild type PLK1 (WT), constitutively active T210D (TD), or kinase-dead K82M (KM) PLK1 mutants. Expression of EMT markers was examined by immunoblotting. (B) Control RWPE-1 and RWPE-1–PLK1 cells were subjected to a wound-healing assay. The bar graph shows calculated percentage of wound closure during 48 hr of cell migration (C) RWPE-1 cells were infected with lentivirus expressing empty vector (EV), wild-type PLK1 (WT), constitutively active T210D (TD), or kinase-dead K82M (KM) mutants. Total cell lysates were subject to immunoprecipitation with CRAF antibody and then analyzed by immunoblotting. p/t: indicates densitometric intensity ratio of phosphorylated to total CRAF. (D) A proposed model of a novel signaling cascade that mediates PLK1-dependent induction of EMT and cell motility.

\*Wu J, Ivanov AI, Fisher PB, Fu Z. Polo-like kinase 1 induces epithelial-to-mesenchymal transition and promotes epithelial cell motility by activating CRAF/ERK signaling. *Elife*. 2016 Mar 22;5. pii: e10734. DOI: [10.7554/eLife.10734](https://doi.org/10.7554/eLife.10734). PMID: [PMCID: PMC4811775](https://pubmed.ncbi.nlm.nih.gov/264811775/)

### About the Investigators

Zheng Fu, PhD, is an Assistant Professor of Human and Molecular Genetics (HMG), and a Member of the Massey Cancer Center (MCC) and the VCU Institute of Molecular Medicine (VIMM), Virginia Commonwealth University, School of Medicine, Richmond, VA. Jianguo Wu is a postdoctoral fellow in Dr. Fu's Laboratory. Andrei I. Ivanov is Associate Professor in HMG and a Member of the VIMM and the MCC. Paul B. Fisher, MPh, PhD, is Professor and Chair of HMG, Director of the VIMM and Thelma Newmeyer Corman Chair in Cancer Research in the MCC.