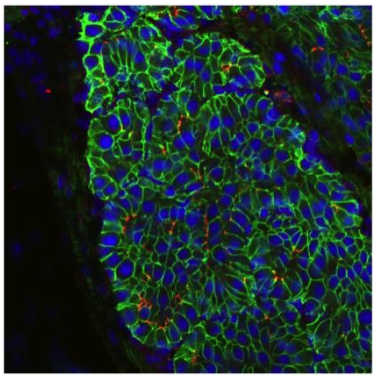
New insight into the regulation of prostate gland morphogenesis



Researchers from the Cell Biology and Stem Cells Unit at CIC bioGUNE, Imperial College London and DKFZ Heidelberg have uncovered a novel link between the tumor suppressor Dkk-3 and TGF-β signaling. The study, by Romero, Kawano et al., is published in the Journal of Cell Science (http://jcs.biologists.org/content/early/2013/02/21/jcs.119388).

Previous studies from the group demonstrated a role for Dkk-3 in human prostate epithelial cells that were cultured in 3D to model aspects of prostate gland morphogenesis (Kawano et al., Oncogene, 2006). The new report shows that Dkk-3 limits cell proliferation in 3D cultures and in the developing mouse prostate. A key observation is that loss of Dkk-3 leads to increased TGF-β/Smad signaling, inhibition of which rescues the Dkk-3 loss-of-function phenotype in 3D cultures. The results are consistent with a model where Dkk-3 is a gatekeeper in the normal prostate, preventing the TGF-β switch from tumor suppression to tumor promotion, and provides further support and rationale for the use of TGF-β inhibitors to treat prostate cancer. These results may also be relevant to other types of cancer where the DKK3 gene is silenced and the response to TGF-β is altered, such as cancers of the breast and ovary.