## The regulation of uncontrolled cell proliferation by hidden switches mediated by RORα

## **Kwang-Hyun Cho**

Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology (KAIST), 291 Daehak-ro, Yuseong-gu, Daejeon 305-701, Republic of Korea.

Cells have evolved molecular interactions that function as switches to prevent undesired proliferative signals. The breakdown of these switches can lead to uncontrolled cell proliferation, which is the hallmark of cancer. We discovered retinoic acid receptor-related orphan receptor (ROR)  $\alpha$ -mediated network switches that are embedded in the extended Wnt signaling network and that can critically regulate the proliferation of colon cancer cells. We found that ROR $\alpha$  mediates cross-regulation between PGE<sub>2</sub> and Wnt signaling, which results in the formation of two network switches: a dose-biphasic switch that turns off the proliferation signal triggered by excessive input stimulation and a hysteresis-inversion switch that converts a hyper-proliferative network state into a hypo-proliferative state. Our results indicate that ROR $\alpha$  is the hidden master regulator at the center of these network switches that critically regulate uncontrolled cell proliferation, thereby providing a promising anti-cancer therapeutic target.