DEC1 regulates breast cancer cell proliferation by stabilizing cyclin E protein and delays the progression of cell cycle S phase

With the support by the National Natural Science Foundation of China and the Ministry of Science and Technology of China, the research team led by Prof. Wu HuiJian (伍会健) at the School of Life Science and Biotechnology, Dalian University of Technology published their recent research result "DEC1 regulates breast cancer cell proliferation by stabilizing cyclin E protein and delays the progression of cell cycle S phase" in *Cell Death and Disease* (2015, 6: e1891).

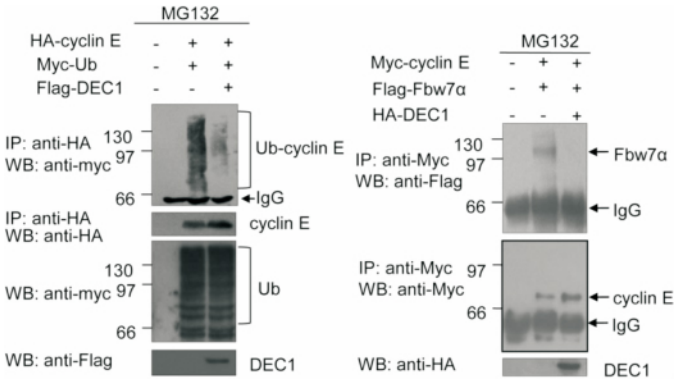

Figure 1 DEC1 upregulates the stability of cyclin E via Fbw7α-mediated cyclin E ubiquitin-proteasome pathway.

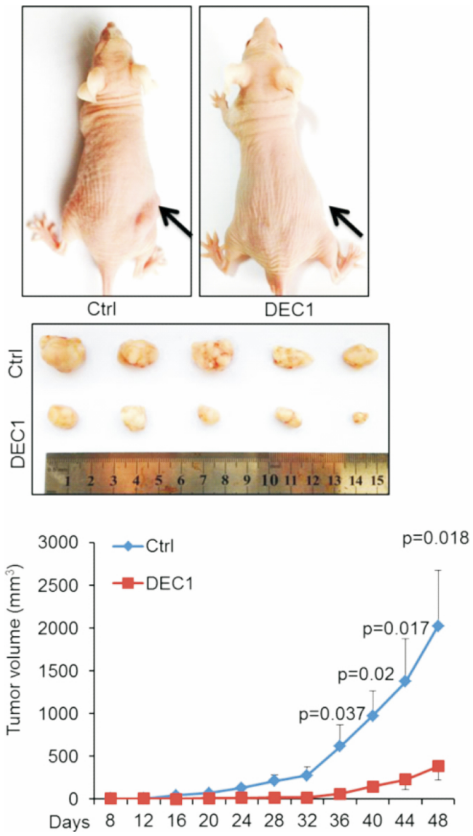

Figure 2 DEC1 inhibits tumor xenograft growth.

Breast cancer that is accompanied by a high level of cyclin E expression usually exhibits poor prognosis and clinical outcome. Several factors are known to regulate the level of cyclin E during the cell cycle progression. The transcription factor DEC1 (also known as STRA13 and SHARP2) plays an important role in cell proliferation and apoptosis. Nevertheless, the mechanism of its role in cell proliferation is poorly understood. In this study, we showed that DEC1 could inhibit the cell cycle progression of breast cancer cells. The cell cycle-dependent timing of DEC1 overexpression could affect the progression of the cell cycle through regulating the level of cyclin E protein. DEC1 stabilized cyclin E at the protein level by interacting with cyclin E. Overexpression of DEC1 repressed the interaction between cyclin E and its E3 ligase Fbw7α, consequently reducing the level of polyunbiquitinated cyclin E (Figure 1). Furthermore, DEC1 also promoted the nuclear accumulation of Cdk2 and the formation of cyclin E/Cdk2 complex, as well as upregulating the activity of the cyclin E/Cdk2 complex, which inhibited the subsequent association of cyclin A with Cdk2. This had the effect of prolonging the S phase and suppressing the growth of breast cancers in a mouse xenograft model (Figure 2). These events probably constitute the essential steps in DEC1-regulated cell proliferation, thus opening up the possibility of a protein-based molecular strategy for eliminating cancer cells that manifest a high-level expression of cyclin E.