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Securin: A Novel Stem/Cancer Stem Cell Marker

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Abstract: Cancer stem cells — the rare cell populations with indefinite proliferative potential and ability to drive the formation and growth of tumors are identified in solid tumors. These cells are known as cancer initiating cells and are capable for self-renewal. These cells are reported to be responsible for drug resistance leading to tumor relapse and recurrence of cancer. It remains unknown how and from where these cells originate. Since, cancer stem cells (CSCs) share common markers and the ability to self-renew- with normal stem cells, it strongly suggests that CSCs might arise from normal stem cells. Several oncogenes are at the epicenter for this phenomenon of putative transformation, formation of precancerous lesions and its subsequent clinical manifestation into mature cancer. While several of these oncogenes are reported to be overexpressed in CSCs, our group has extensively studied 'securin' alias 'pituitary tumor transforming gene' (PTTG) as one of the putative oncogenes reportedly overexpressed in almost all the tumors including ovarian tumors studied to date. It is a multi-domain and multifunctional proto-oncogene, and plays critical role in separation of sister chromatids during cell division. Its overexpression is linked to cellular transformation, gene instability, aneuploidy, tumor progression, invasion, metastasis, cancer recurrence and oncotherapy resistance. In our studies, we demonstrated co-expression of securin with several stem cell/cancer stem cell markers, pluripotent and germ stem cell markers in normal ovary, various stages of ovarian tumor (Benign, Borderline and High Grade), and in ascites cells collected from patients with recurrent ovarian cancer. Knockout of securin in ovarian cancer cell line (A2780) showed regulation of expression of several stem/cancer stem cell markers, and regulation of self-renewal signaling pathways including Notch1, WNT1/β-catenin and SHH. From our results, we conclude that securin is a novel stem/cancer stem cell marker and plays important role in regulation of stem/cancer stem cell population.

Keywords: Stem cells, Cancer stem cells, Ovarian cancer, Securin, Oncotherapy.

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