

# SOX2OT, a long non-coding RNA involved in autophagy regulation

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## Abstract

SOX2 overlapping transcript (SOX2OT) is a long non-coding RNA associated with cancer pathogenesis. It contributes to a variety of cellular functions and recent evidence propounds its association with autophagy process. It has been showed that SOX2OT can regulate the expression of different autophagy associated factors in human cells with different mechanisms, however more remains to be investigated.

**Keywords:** SOX2OT, lncRNA, Autophagy

## Statement

Human SOX2OT, located in chromosome 3q26.3 encodes for a non- protein coding long RNA with different alternative splice variants (1). It was discovered as a gene associated with eye developmental disorders including microphthalmia and anophthalmia (2). The function of SOX2OT has been under

investigation since its discovery. It has been shown that SOX2OT can regulate the embryonic stem cell in vertebrate (3) and also it has higher expression level in different tumor types taking role in pathogenesis of cancers(4).

Recently it was reported that SOX2OT can control the autophagy in osteosarcoma (5),

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pheochromocytoma cell (6), human podocytes cells (7). Autophagy is a conserved cellular homeostasis mechanism under stressful condition. It involves in pathogenesis of different disease like infections, neurodegenerative disease and cancer (8). Of notice, autophagy is a fundamental process in lens fiber cells which SOX2OT shows high expression level (3).

SOX2OT variant 7 overexpressed osteosarcoma cell showed higher autophagy associated gene expression (Atg5, Atg7 and Beclin1), increased LC3-II/LC3-I ratio and decreased autophagy substrate P62; indicating SOX2OT variant 7 over expression can induce autophagy in osteosarcoma cell lines (U2OS and SaoS2). Overexpression of SOX2OT in osteosarcoma cancer stem cells contributes to stemness and Doxorubicin and Epigallocatechin Gallate (EGCG) toxicity (5).

In a recent study in the human podocytes exposed to hyperglycemia, it has been reported that SOX2OT knockdown can decrease the Beclin-1 and Atg7 expression level, but an increase in p62 cellular level. In contrast, ectopic overexpression of SOX2OT deposited autophagy induction in human podocyte cells. It was illustrated that SOX2OT can decrease miR-9 inhibitory effect on SIRT-1 (autophagy inducer) by functioning as a Competing endogenous RNA, leading to enhanced autophagy. Accordingly it was postulated that, SOX2OT can attenuate human podocytes injury from hyperglycemia through autophagy related mechanism (7)

In other hand SOX2OT suppression can protect pheochromocytoma cells (PC2) from H<sub>2</sub>O<sub>2</sub> induced injury through a mechanism associated to autophagy inhibition. SOX2OT

knocked down PC2 cells showed less Beclin-1 overexpression and p62 decrease under H<sub>2</sub>O<sub>2</sub> treatment. Further investigation showed SOX2OT knockdown mitigates H<sub>2</sub>O<sub>2</sub> induced injury via upregulation of miR-211 (6).

The above mentioned evidence highlights the importance of SOX2OT function in autophagy regulation in different conditions. Regarding the high expression of SOX2OT in human CNS and eye, it is worthy to study its association with autophagy related neuronal and eye disease; however the clear mechanism of autophagy regulation by SOX2OT needs more investigations.

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