論 文 要 旨

S100A16 up-regulates Oct4 and Nanog expression in cancer stem-like cells of Yumoto human cervical carcinoma cells

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Cancer stem-like cells (CSCs), which possess the ability to self-renewal and are multipotent, are regarded as the cause of tumor formation, recurrence, metastasis and drug resistance. It is necessary to understand the properties of CSCs in order to treat them effectively. It has been previously reported that S100 family proteins, which carry calcium-binding EF-hand motifs and are associated with tumorigenic processes, serve crucial roles in maintaining cancer stem-like properties. S100A16 is upregulated in various types of cancer, including bladder, lung and pancreatic. However, the roles of S100A16 in cancer cells, particularly CSCs, are not clear. The present study investigated the roles of S100A16 in CSCs using the sphere formation assay of Yumoto cells, which are a human cervical carcinoma cell line. The mRNA expression levels were evaluated by reverse transcription-polymerase chain reaction and the protein expression levels were detected by western blot analysis. Following the sphere formation of Yumoto cells, the mRNA and protein expression level of Oct4, Nanog and S100A16 were increased compared with the control cells. Following transfection with S100A16 small interfering RNA (siRNA), the mRNA and protein expression of Oct4 and Nanog were decreased and the spheroid size was significantly decreased in the sphere formation of Yumoto cells compared with control siRNA treated cells. There was no change in the p53 mRNA expression level, whereas the p53 protein

expression level, which was decreased by the sphere formation, was recovered by S100A16 knockdown. In addition, the protein expression levels of Oct4 and Nanog, which were increased in the sphere formation, were decreased by the proteasome inhibitor lactacystin. No differences were observed in the S100A16 protein expression between the presence or absence of lactacystin. These results suggest that S100A16 serves an important role in the CSCs of human cervical carcinoma and is a positive regulator of Oct4 and Nanog.