



Development of a novel therapy for intractable diseases by targeted intracellular delivery of cytokine signal inhibitor (SOCS) *in vivo*

Outline

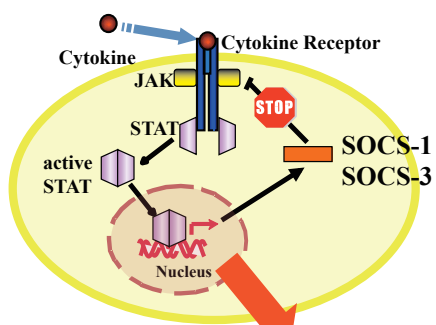
Dysregulated cytokine signaling is associated with development and progression of cancers. This study was aimed to investigate whether the gene delivery of suppressor of cytokine signaling (SOCS), a family of negative regulators of cytokine signaling, in cancer cell is effective in inhibition of cancer cell growth *in vitro* or *in vivo*. We also examine the detailed mechanism of action of SOCS molecules on cancer cells.

Our current target is malignant pleural mesothelioma (MPM), an asbestos-related pleural tumor with a poor prognosis. By means of adenoviral gene delivery of SOCS3 into MPM cells *in vitro* and *in vivo*, we will determine whether SOCS-mediated therapy is a promising strategy to treat cancers. We also are planning for a clinical trial of AdSOCS3 for the therapy of human MPM.

Expected Outcome

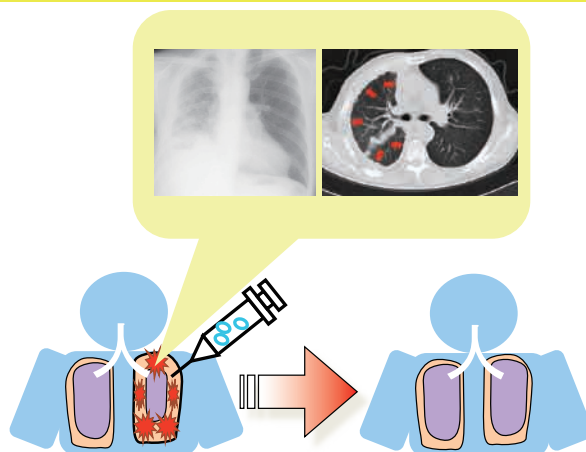
The number of MPM patients is rapidly increasing and is supposed to peak at 2030. However, because MPM is rarely resectable and is also highly resistant to chemotherapy, no curative therapy for MPM has not been established. Our preclinical study indicates that intrathoracic injection of adenovirus vector expressing SOCS3 (AdSOCS3) is a promising strategy to treat human MPM. Our study is thus of clinical and social importance to provide a basis for the development of novel therapy for MPM and possibly other intractable cancers.

Cytokine signal inhibitor SOCS as a novel anti-cancer agent



Naka et al., 1997, Nature

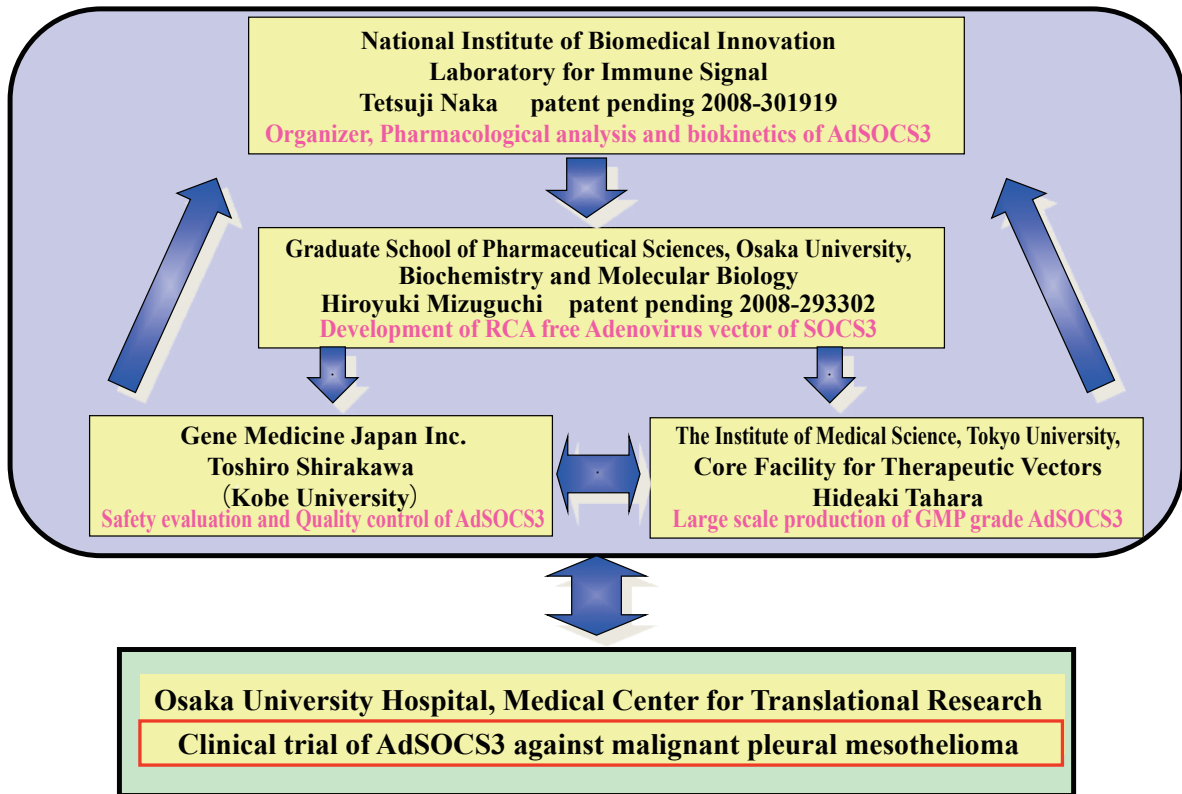
- Proliferation (→Cancer)
- Activation (→Autoimmunity)



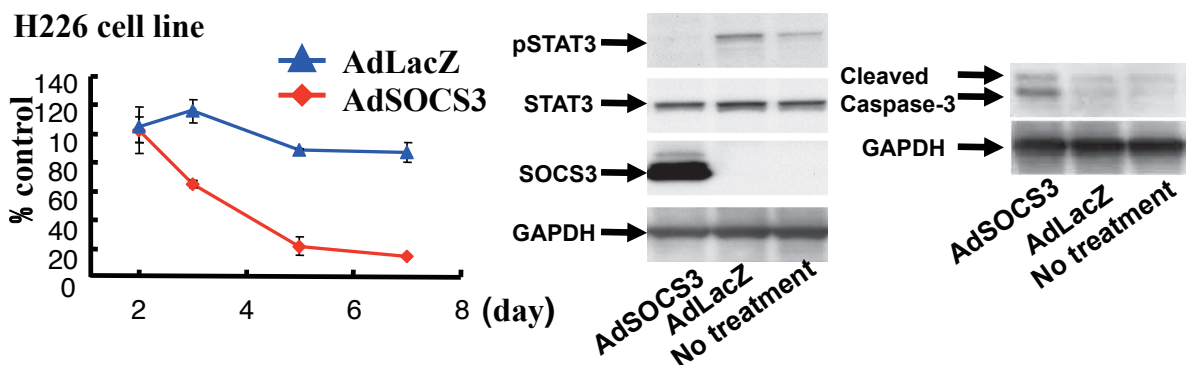
• SOCS molecules are inhibitors of cytokine signaling and their defects result in dysregulated intracellular signaling and tumor development. Intracellular delivery of SOCS may be effective to prevent proliferation and metastasis of cancer cells.

• Malignant pleural mesothelioma (MPM) is an intractable disease without established therapy. We develop a novel and safe gene therapy by intrathoracic administration of AdSOCS3 (SOCS3-containing adenovirus vector with low antigenicity) .

System



Enforced expression of SOCS in vitro potently inhibits proliferation of malignant pleural mesothelioma (MPM) cell lines and induces their apoptosis.



Anti-cancer effect of SOCS in vivo : SOCS can inhibit tumor growth in a murine model of MPM.

