



ידע חברה למחקר ופיתוח בע"מ

מסחור טכנולוגיות של מכון ויצמן למדע

YEDA RESEARCH AND DEVELOPMENT CO. LTD.

TECHNOLOGY TRANSFER FROM THE WEIZMANN INSTITUTE OF SCIENCE

Identifying and Targeting Senescent Cells:

Therapeutic elimination of senescent cells

Project Number:	1825
Principal Investigator:	Prof. Valery Krizhanovsky
Patent Status:	Pending
Last Updated:	18-06-2018 (1)

Overview

A novel panel of cell surface markers for targeted elimination of senescent cells as a potential treatment for fibrotic conditions.

Background and Unmet Need

Cellular senescence is a form of cell-cycle arrest, which can be triggered in many cell types, and short-term induction of senescence can be beneficial due to its anti-tumorigenic properties. However, long-term senescent cell induction can lead to numerous problems, such as promoting tumorigenesis and metastasis in a cell non-autonomous manner, and contributing to tissue aging – from tissue dysfunction to hair loss tissue. Moreover, senescent cells promote tissue inflammation and fibrosis, and are therefore related to development of fibrotic diseases as well. **Consequently, there is a strong need for diagnostic and therapeutic tools that can recognize and eliminate senescent cells.**

The Innovation

The group of Prof. Krizhanovsky **performed proteomic analysis of senescent cells and discovered a set of cell surface proteins that are expressed when cell senescence is induced.**

The Technical Essence:

The Krizhanovsky team induced senescence of mammalian cells by either DNA Damage Induced Senescence (DIS) or infection with an oncogene leading to Oncogene-Induced Senescence (OIS). DIS and OIS cells were then examined for senescent properties, after which their cell surface proteins were isolated and sent for mass spectrometry analysis (see figure below). A set of proteins were found to be unique and shared by both DIS and OIS cells. From the shared proteins, Protein "X" was further examined, as the protein is known to be an intra-cellular protein in healthy cells but was shown by the Krizhanovsky team to accumulate on the surface of senescent cells in a time-dependent manner. The specificity of Protein X as a cell surface marker for senescent cells was confirmed by flow cytometry, single cell analysis, and other means. Additionally, the Krizhanovsky team has also begun preliminary work to determine the biological role of Protein X.

Applications and Advantages:

- **Novel cell surface markers** – Unique identifier proteins for senescent cells.
- **Diagnostic tool** – enables to identify senescent cells and diagnose related diseases.
- **Therapeutic tool** – delivering agents to senescent cells by targeting these cell surface proteins in the treatment of numerous indications.

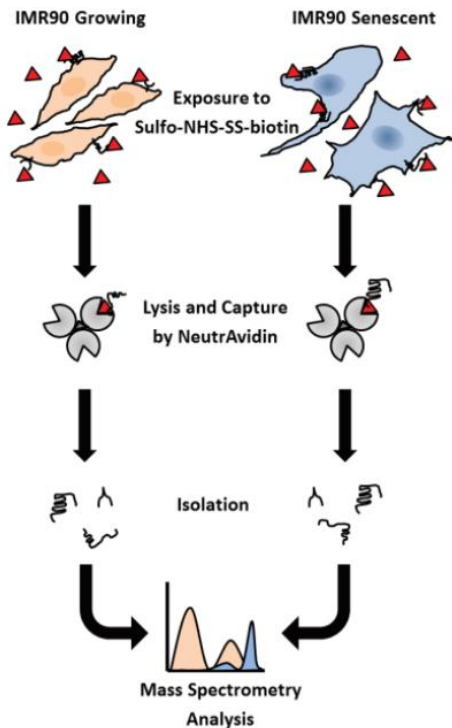


Diagram of the procedure used by the Krizhanovsky group to identify the unique cell-surface Protein X, found to accumulate on the cell surface of senescent cells.

Development Status

Prof. Krizhanovsky and his team discovered senescence-specific cell surface markers via usage of *in vitro* models, and verified their relevancy to *in vivo* disease settings. Currently, efforts to develop a monoclonal antibody that would target protein "X" are taking place. The antibody is developed as means for targeted elimination of senescent cells via antibody triggered mechanisms.

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