Senescence

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Machine learning algorithm predicts senescence

Cellular senescence is one of the main mechanisms to prevent the replication of unhealthy cells, arresting their replication and limiting the spread of DNA damage. During the life of an individual, the pathological accumulation of senescent cells leads to aging and diseases. Although senolytics have great therapeutic potential to prevent aging and disease, reliable components have yet to be found. Triggering senescence could also be a potential approach for treating cancer, but drugs that selectively induce senescence in cancer cells have yet to be identified. A study in *Nature Communications* shows the capabilities of machine learning (ML) algorithms to better detect senescence and screen for senolytics and drugs that induce senescence.

A key requirement for senolytic drug screening is the ability to accurately identify senescent cells. Using microscopy images of cell cultures, the researchers trained a ML algorithm to distinguish senescent lung cells from healthy lung cells based on nuclear features. Additionally, the ML algorithm was capable of distinguishing senescent cells from DNA-damaged and quiescent cells in vitro. Then, the algorithm showed good detection rates, accurately identifying senescent cells from cell cutures derived from multiple tissues. Given the good detection rate of the algorithm, the team next assessed if it could assist in the detection of senotherapies. First, using known senolytic drugs to treat cell cultures, the team verified that the algorithm could accurately identify when drugs were applied. Then, the team screened chemotherapeutic drugs in cancer cell cultures, using the classifier algorithm to help identify the most efficient senotherapies. To further characterize the algorithm's capabilities, the team used the algorithm to detect senescence in tissue sections. Here, the algorithm showed efficiency in detecting senescence in the liver of a mouse model of cancer and measuring the efficacy of senolytic drugs in these animals. The algorithm was also useful for predicting senescence-associated liver fibrosis and aging in mice. Finally, researchers demonstrated the applicability of the algorithm to human samples, as it successfully predicted senescence in the human tissue affected by non-alcoholic fatty liver disease.

This proof-of-concept study shows that ML can be a valid tool for scoring senescence in a multitude of samples, from cell culture to animal and human tissues, which could facilitate the discovery of new efficient senotherapies in the future.

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