Development of a 3D in vitro lung cancer model for immuno-oncology

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Abstract

Every year, lung cancer is the most frequently diagnosed cancer in men and women. Even though the recent introduction of targeted therapies has greatly extended the treatment options, the vast majority of patients (80%) eventually develop resistance, leading to more than 1 million deaths worldwide. This dramatic observation underscores the inability of current therapeutic classes to treat the disease. Research is now focusing its hope on immuno-oncology, a strategy that involves the reactivation of patient's immune system to fight the tumors. This approach sounds very promising as it supposes the destruction of tumors without causing any toxicity to normal tissues as well as the installation of a long-term memory to prevent the recurrence of the disease. As a result, it is mandatory to set up new preclinical models which will be useful both to elucidate the complex mechanisms deployed by tumors to escape immune surveillance and to test new immuno-oncology drugs. To tackle this challenge we propose to develop an in vitro immunocompetent model for lung cancer. To that end, we will use tissue-engineering methods to reconstitute a functional respiratory epithelium invaded by tumor nodules, starting exclusively from human cells. These micro-tissues will also contain lung fibroblasts, macrophages and dendritic cells to recapitulate the cellular complexity found in tumor microenvironment. Such a model will allow reproducing in vitro the interactions between tumor cells and key components of the immune system. Thus, by closely mimicking the patient situation, these human immunocompetent tumor micro-tissues will permit to better identify future cancer treatments while sparing the life of many animals used for experimentation.