

IMMUNOLOGY AND CANCER THERAPY

Accepted Abstract

May 22-23, 2019 | Rome, Italy

Immunol Case Rep 2019, Volume 3 | DOI: 10.4066/2591-7366-C2-006

NOVELTIES IN ADDITIVE MANUFACTURING AND BIO-PRINTING

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Here, author describes a unique strategy designed to identify dominant tumor antigens associated with lung cancer cells. Vaccines that induced immunity to dominant tumor antigens can induce therapeutic immune responses in tumor bearing mice and patients. In a squamous carcinoma mouse model of non-small cell lung cancer, the antigen-discovery strategy, this is based on the finding that genes encoding dominant tumor-associated antigens (TAA) (immunity to dominant tumor antigens can lead to tumor regression) are expressed in a highly immunogenic form by a non-malignant, allogeneic fibroblast cell line transfected with a cDNA expression library from lung cancer cells. The transfected cells, which express the products of multiple genes specifying an array of antigenic determinants, including genes specifying dominant tumor antigens were selected for antigen discovery. However, as only a small proportion of the transfected cell population was expected to have incorporated gene-segments that specified TAA (the vast majority specified normal cellular constituents), a unique strategy was developed that resulted in the identification of Cyp2e1, a derivative of cytochrome p450, as an immune dominant tumor antigen in murine squamous carcinoma cells and growth factor receptor bound protein 10 GRB10 and Trop1 as immune dominant tumor antigens in murine breast cancer cells. The strategy consisted of dividing aliquots of the suspension of transfected cells into 10-15 small pools (initial inoculums 10E3, using a 96 well cell culture plate was used for this purpose, allowing the cells from each pool to increase in number (to approximately 10E7,) small starting inoculums increase the likelihood that some pools will contain greater numbers of cells that express dominant cancer antigens than others). Afterward the transfected cell-populations from each pool were divided into two portions. One portion was maintained frozen/viable for later recovery. The remaining portion was co-incubated with (mitomycin C-treated) squamous carcinoma cells. Two independent assays, (ELISPOT interferon gamma-release and 51-Cr release cytotoxicity) were used to identify pools that stimulated immunity to the squamous carcinoma cells to the greatest, (and for later use and as a control) to the least extent. Frozen cells from these pools were re-established in culture; the cell-numbers were expanded and subdivided for additional rounds of immune selection (They reasoned that if the starting inoculums were sufficiently small, then randomly, some pools would contain greater numbers of cells that induced the anti-tumor immune response than others). After further rounds of immune selection, microarray was used to identify the products of genes over-represented in the cell pool that stimulated the antitumor immune response to the greatest and (for use as a control) to the least extent.



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