

## Technology Offer

# Expression of immunoglobulin-cytokine fusion proteins in malignant B cells

Reference Number: TO 01-00176



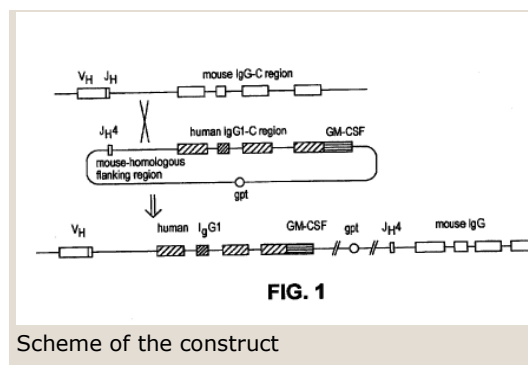
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## Challenge

The immunoglobulin idiotype expressed on B cell lymphomas is a tumor-specific antigen which however shows a low immunogenicity in the host bearing the tumor. Several approaches have been and are evaluated to induce an immune reaction against the idiotype, amongst others, the idiotype has been coupled to GM-CSF to be used as a soluble protein for vaccination. GM-CSF is able to recruit professional antigen-expressing cells and leads to an effective presentation of the idiotype and, thus, to activation of T cells. This approach bears the disadvantage that the immunoglobulin V genes of the lymphoma have to be cloned and the fusion protein has to be produced in vitro and purified. In a clinical situation, this would require to prepare individual vaccines for each patient.

## Technology

The vectors provided according to the invention enable site-specific insertion of the cytokine (GM-CSF) gene by homologous recombination into the heavy chain locus of immunoglobulin



genes without any need to isolate the V gene and to insert the gene into the vector. The vector is directly incorporated into the malignant B cell and the expression is induced in the cell. Such altered tumor cells may be administered directly to the patient. The vector may also be employed in an ex vivo assay. Cultured dendritic cells are induced to present tumor-specific peptides and optionally also to activate T cells by means of the fusion protein expressed by the recombinant tumor cells. The antigen-presenting cells or the

activated T cells would then be reintroduced into the patient.

## Commercial Benefit

The solution according to the invention does not only save time, effort, and costs but also leads to a significantly better tumor-protective effect. The novel vectors may be employed universally in patients without the need to prepare individual vaccines. The vector described may be potentially used for all lymphomas.

## Development Status

The benefit of the modification of a lymphoma idiotype for anti-tumor immunization is demonstrated using murine B cell lymphoma and immunization of mice. The immunized mice show a significant advantage of survival.

## Patent Situation

Patents are granted in the US (US 6,673,573), Europe (EP0874054), and Japan (JP03802677), a US-divisional application (US 2004/0072300) is pending.

## Commercial Opportunity

License is being offered on an exclusive basis. In addition, cooperation can be offered and will be strongly desired.

## Relevant Publications

Selmayr et al. (1999), Gene Therapy 6, 778-784.

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