



Prognostic test for treatment of diffuse large B-cell lymphoma

Information Summary

| | |
|----------------------|--|
| Reference Code: | ROI 05041 |
| Technology overview: | VAV and Phosphorylated ERK as biomarkers for the response to CD40 antibody treatment of Non Hodgkin's lymphoma patients with diffuse large B-cell lymphomas (DLBCL). |
| Applications: | Prognostic test to evaluate the response of Non Hodgkin's Lymphoma patients to anti-CD40 therapies |
| Validation: | Markers validated in CD40 responsive and non-responsive cell lines. Detection and variation of biomarkers observed in tumor biopsies. |
| Ideal receptor: | Major pharmaceutical firm, CRO, or imaging specialists. |
| Inventors: | Robert Sladek, Thomas Hudson et. al |
| Opportunity: | A solution to stratify responsive from non patients. |
| Contact: | Giovanna Sebastiani, Ph.D. 514-398-6138 giovanna.sebastiani@mcgill.ca |

Technology Description

The incidence of non-Hodgkin's lymphoma has increased over two-fold in the past 20 years, and is now the 5th most common malignancy in North America. 40% of these tumors are diffuse large B-cell lymphomas (DLBCL).¹ Standard treatments for DLBCL include multi-agent chemotherapy, radioimmunotherapy, and high-dose chemotherapy followed by stem-cell transplantation.² Current regimens achieve a five-year survival of only about 40%.¹ Antibodies against CD40 can induce apoptosis in malignant B-cells, and are therefore an attractive

possibility for targeting B-cell lymphomas. However, the response to CD40 stimulation is variable even within the same tumor type. Though some of these tumors respond to CD40 stimulation by undergoing apoptosis, a proportion of these do not respond to the treatment or worse still can be stimulated to survive and proliferate and become resistant to chemotherapeutic agents.³

The McGill researchers have demonstrated that diffuse large B-cell lymphoma cell lines containing VAV and phosphorylated ERK were susceptible to CD40-mediated cell death, whereas cell lines lacking these two markers showed no response. Also, inhibition of ERK phosphorylation blocked CD40-mediated cell death, thereby confirming the correlation.³ VAV and phosphorylated ERK have also been detected by immunohistochemistry in paraffin-embedded human biopsy material and have been shown to exhibit variation in expression levels among tumors.

Market Need and Opportunity

Anti-CD40 drugs are currently under clinical trial for various indications. Though it is known that these drugs could be effective against DLBCL, a condition for which the prognosis is very poor, variation in response to the drug prevents its utilization for the treatment of DLBCL. The current technology provides a solution to identify responsive patients and therefore could provide an opportunity to use the drug for this indication

Additional Reference Material

1. Fisher SG, et al., 2004, *Oncogene* 23: 6524-34.
2. Long, J et al., 2006, *Semin Oncol Nurs* 22: 97-106.
3. Hollmann CA, et al., 2006, *Cancer Res* 66: 3550-57