

Sensitive PCR-based Biomarker for Identification of Residual Hodgkin Lymphoma Cells

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Challenge

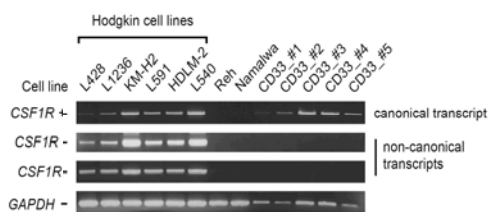
Hodgkin Lymphoma (HL) is one of the most common lymphomas in the Western world. Usually it is derived from B lymphoid cells of the hematopoietic system. The incidence of HL amounts to 2 to 4 cases among 100.000 persons. HL is diagnosed, i.a. by biopsy of lymph nodes and bone marrow, CT scan, X-ray and ultrasonics. Out of this analysis a therapeutic scheme for the treatment of HL-patients usually with chemotherapy and/or radiotherapy is developed. Therapeutic success is monitored by the same means as used for diagnosis.

In particular HL-patients can be treated successfully in the early stages of disease. But it's difficult to stratify the risk and to detect residual tumor cells e.g. in the bone marrow, which might a highly relevant diagnostic and prognostic marker. At present biopsy specimens from HL-patients are primarily analyzed by immuno-histochemical staining, a time-consuming technical approach, which requires expert know-how. Therefore a biomarker detectable via a simple RT-PCR approach would be most suitable to reduce costs, save time and to detect HL-cells in e.g. bone marrow in an easy and sensitive technical approach.

Technology

In recent studies, an aberrant expression of the colony-stimulating factor 1 (CSF1R) has been described. Now, it has been demonstrated that this over-expression is stimulated by a long terminal repeat (LTR) promoter upstream to known CSF1R promoter. This aberrant LTR-activation leads to an aberrant CSF1R mRNA transcript

The LTR-*CSF1R* transcript could be identified in all samples of HL patients (6 cell lines and 3 tissue samples) and in 4 of 5 anaplastic large cell lymphoma (ALCL) specimens.



Analysis of LTR-CSF1R in HL cell lines and other cell lines. GAPDH was analyzed as control.

Remarkably, the LTR-*CSF1R* transcript could not be found in any of the analyzed control samples of healthy donors. Furthermore it was not detectable in 25 non-HL samples, like diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma and B-cell chronic lymphocytic leukemia. For HL this seems to be the first specific marker which can be detected via a PCR approach. This biomarker opens up the possibility to screen in a fast and technical simple manner tissue from HL-patients, e.g. bone marrow, for resident or even residual HL cells.

The present invention therefore offers new options to:

- detect HL and/or ALCL cells in a very sensitive way, e.g. before, during and after treatment of patients
- validate the success of the therapy by screening for residual HL and/or ALCL cells

Commercial Opportunity

- In-licensing of IP for developing a diagnostic assay

The inventors are open for any collaboration for validation and development of the use of the biomarker; they have excellent clinical access to patients.

Patent Situation

An EP patent application has been filed in 2009, a PCT application is pending.

Further Reading

Nature Medicine, May 2010, Lamprecht et al.

Berlin
Braunschweig
Hamburg
Hanover
Munich
Neuherberg

Ascenion GmbH
Herzogstraße 64
D-80803 Munich
T +49 (0) 89 31 88 14 - 0
F +49 (0) 89 31 88 14 - 20
info@ascenion.de
www.ascenion.de