Technology Offer

Ref.-No. M12/12

Methods and peptides for preventing and treating BCR-ABL and c-ABL associated cancer diseases

Introduction

The leukemia forms chronic myeloid leukaemia (or chronic myelogenous leukaemia; CML), acute lymphatic leukaemia (ALL) and acute myeloic leukaemia (AML) have been described as diseases caused at least in part by a reciprocal translocation between chromosomes 9 and 22, which cytogenetically results in the Philadelphia chromosome (Ph) and molecularly gives rise to the chimeric BCR-ABL1 gene. More than 95 % of patients suffering from CML, which is characterized by increased and unregulated proliferation of predominantly myeloid cells in the bone marrow, have been tested positively for the BCR-Abl fusion protein resulting in a high and unregulated Abl tyrosine kinase activity. Currently used treatments against CML that test positively for BCR-Abl include, in addition to general cytostatics and potential stem cell transplantation, several different tyrosine kinase inhibitors like Imatinib (Gleevec) for down-regulation of increased tyrosine kinase activity. Although inhibitors like Gleevec show curative properties during the early chronic phase, a promising therapy for patients in the later phases of the disease has not yet been discovered. Additionally, existence or rapid occurrence of drug resistance during treatment further limits the use of such inhibitors.

Patent situation

Patent application filed in Europe. Granted patent in USA.

Invention

The invention provides a protein sequence with strong inhibitory properties against the c-Abl kinase activity. On investigating the interplay between the viral proteins of influenza viruses and host cell proteins, we discovered a massive inhibtion of c-Abl kinase activity driven by the viral non-structural protein 1 (NS1). Thereafter, we analyzed the sequence motifs in NS1 required for inhibtion of c-Abl. The discovered sequence motifs therefore could be used for the development of a peptide or peptidomimetical approach to treat and potentially cure BCR-Abl mediated disease.

Advantages of the invention

- stronger inhibtion of c-Abl compared to currently used inhibitors
- different mode of action (protein-protein interplay), potentially reduces risk of resistance development
- potential for specifically targeting affected cells, resulting in less side effects
- gene therapeutic potential for long term cure of disease
- new, highly innovative and promising approach to treat BCR-Abl driven disease

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