URVentures

Methods to Inhibit the Progression of Follicular Lymphoma

Methods for obtaining specific and non-toxic inhibitors of Activation Induced Deaminase (AID) nuclear import that prevent progression of follicular lymphoma (FL), once diagnosed.

Problem Solved by this Technology

Activation Induced Deaminase (AID) causes DNA mismatch mutations. In B cells, AID's heavily-regulated activity facilitates antibody diversification, but when it becomes unregulated for some reason, the mutation process leads to FL and other types of cancer. FL is considered a chronic illness with a relapsing and remitting pattern. It is, therefore, managed with close observation and chemotherapy. There is no gold-standard treatment, and it remains a manageable, but incurable disease.

Applications

Researchers at the University of Rochester have developed methods comprised of two novel fluorescence-based live cell assay screens to identify AID nuclear import inhibitors that do not have off-target toxic effects. AID-specific nuclear import inhibitors identified by the screens prevent nuclear entry, limit the access of AID to genomic DNA, and inhibit AID mutagenic activity. These AID-selective inhibitors compounds have the potential to become new anti-cancer agents preventing progression of certain types of cancer. In FL, these agents might keep patients in remission for longer periods preventing progression of cancers wherein chromosomal translocation and recombination are associated with advanced stages and grades.

Intellectual Property Status

Patent application pending in the United States.

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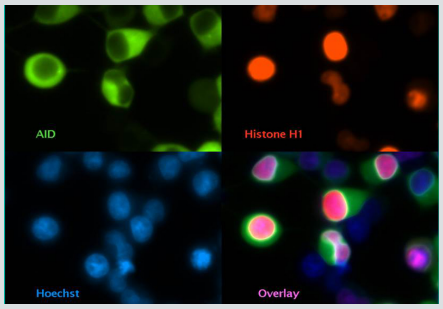

Under steady state conditions more AID appears in the cytoplasm than in the nucleus. AID's nuclear localization signal, NLS is composed of basic residues dispersed in four clusters and is different than the canonical NLS composed of a bipartite organization of basic amino acids. AID may therefore have a 'conformational NLS' composed of interactions of the individual charged regions to form a super-secondary structure. This different and fold-dependent NLS may make AID highly amenable to a strategy of selective nuclear import inhibitor. Fluorescent live cell assay methods that evaluate changes in AID nuclear localization relative to a permanent nuclear protein such as Histone H1 can be used to screen for anti cancer hits that uniquely affect AID-dependent cancers.

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