

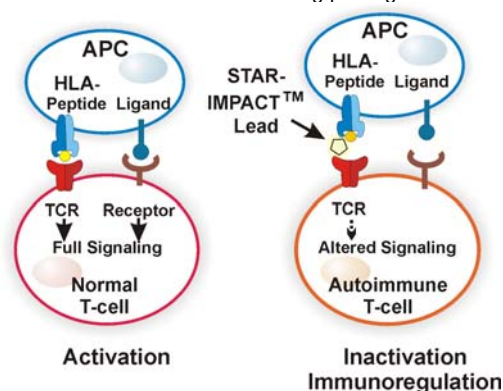
STAR-IMPACT™ Screening

Orally Active Immunosuppressants for Autoimmune Diseases

Altor is employing its STAR-IMPACT™ screening platform to identify and develop small molecule compounds that block T-cells involved in the autoimmune response. Altor has established proof-of-principle in identifying small molecule leads that antagonize HLA-A2-stimulated T-cell responses *in vitro* and *in vivo*. In addition, an integrated screening program is in place to characterize inhibitors of other HLA molecules associated with autoimmune diseases.

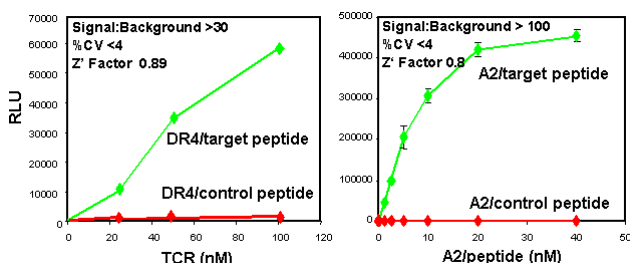
Background

T-cells play an important role in autoimmune diseases, organ transplant rejection and graft-versus-host disease. T-cell activity is controlled by the interactions between T-cell receptors (TCRs) and their cognate MHC-peptide molecules. Altor has developed its STAR-IMPACT™ screening platform to identify and characterize compounds that specifically inhibit these interactions as a means of controlling pathogenic T-cell responses.



STAR-IMPACT™ screening platform targeting HLA molecules

Novel TCR and MHC-peptide production techniques have enabled Altor to assemble sensitive, specific screening methods to identify compounds that block TCR interaction with the MHC-peptide complex. Particular focus is being placed on interactions involving human MHC molecules associated with autoimmune diseases or other immune disorders. For example, high-throughput screening (HTS) assays have been developed using the AlphaScreen detection system to identify small molecule inhibitors targeting HLA-DR4, an MHC allele associated with rheumatoid arthritis, multiple sclerosis, and type I diabetes; HLA-DR2, an MHC allele associated with multiple sclerosis; and HLA-A2, the most prevalent human MHC allele. By targeting only the subset of MHC molecules associated with disease, IMPACT™ therapeutics are not expected to have generalized immunosuppressive effects on protective T-cell responses.



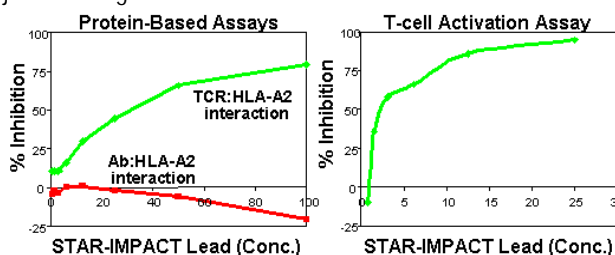
Homogeneous screening assays for MHC-peptide:TCR interactions

Altor has screened a diverse library of small molecule chemicals in its primary protein-based HTS assays. Inhibitory compounds discovered in these screens are being further characterized for potency, specificity, and toxicity using T-cell based activation assays. Both the protein- and cell-based assays are simple and fully automated and can be readily scaled-up to screen large libraries. Lead molecules identified by this process are

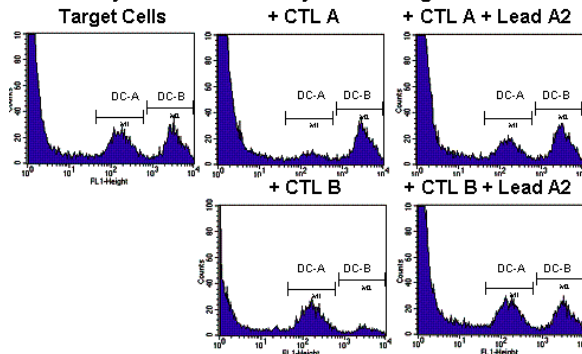
then tested for immunosuppressive activity and toxicity in HLA-transgenic animal models.

Proof-of-principle established

Altor has already identified a number of lead compounds that 1) inhibit TCR:HLA-A2-peptide molecular interactions, 2) reduce immune responses of HLA-A2 specific T cells *in vitro*, and 3) are non-toxic. Several of these compounds have also been shown to inhibit HLA-A2-specific cytotoxic T-cell responses in transgenic animal models. These antagonists are readily amenable to drug optimization and could form the basis of novel treatments for multiple sclerosis, type I diabetes, graft rejection and graft-versus-host disease.



Cytotoxic T-cell Activity in HLA-A2 tg Mice



Small molecule leads inhibit HLA-A2 activity *in vitro* and *in vivo*

In addition, Altor has expanded its STAR-IMPACT™ screening platform to identify HLA-DR antagonists that could lead to the development of orally administered drugs to treat rheumatoid arthritis, multiple sclerosis and other DR-associated autoimmune diseases.

Intellectual Property

Altor has assembled broad, integrated patent positions for its STAR™ and IMPACT™ technologies that include 30 issued U.S. and foreign patents and 57 pending patent applications. This intellectual property estate provides Altor with a strong and leading position for generating novel and versatile classes of targeted therapeutic reagents.

Corporate Strategy

Altor's corporate strategy is to continue to build value through internal drug development programs while exploring new licensing and funding opportunities for diagnostic/therapeutic product technologies.

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