Computational Discovery and Experimental Validation of Novel Drug Targets in Immuno-oncology

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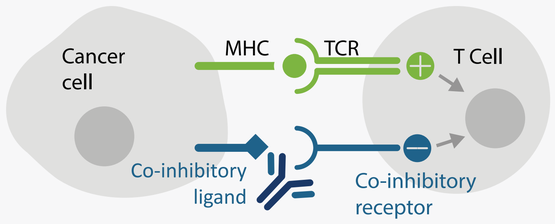
Introduction

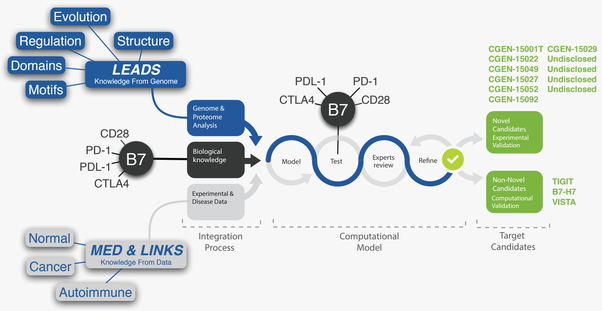
Immuno-oncology represents a paradigm shift in the treatment of cancer. In 2010 we directed our predictive discovery spotlight on the field of immune checkpoints as the Company's first focused application of its discovery infrastructure, with a goal of addressing the unmet need for novel, effective cancer immunotherapies.
Within a few months of predictive discovery work, we significantly enriched the more than twenty-year-old field of immune checkpoints with the discovery of eleven novel immune checkpoint drug target candidates.
Today, our unique predictive discovery capabilities have resulted in one of the broadest and most promising novel target pipelines for immuno-oncology in the industry. Our pipeline includes multiple opportunities for first-in-class therapeutics addressing areas of unmet medical need in oncology.



B7 Discovery Platform

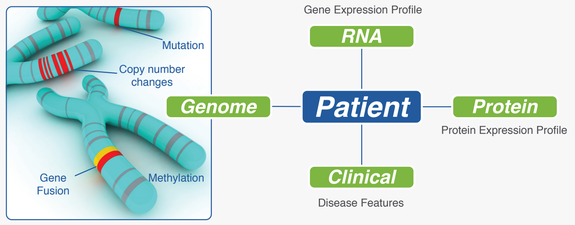
Compugen's discovery process has been optimized for over a decade and proven on a variety of biological phenomena. The discvoery process is based on three pillars, biological knowledge derived from the literature, function prediction derived from DNA and protein sequence analysis (LEADS platform) and analysis of vast numbers of experimental molecular data sets (MED platform).

The Discovery of novel B7/CD28-like immune checkpoints is based on unique features identified for existing known B7 immune checkpoints. The B7 discovery model is an integrative model of 4 features and is primarily a genomic discovery algorithm.



LINKS Platform

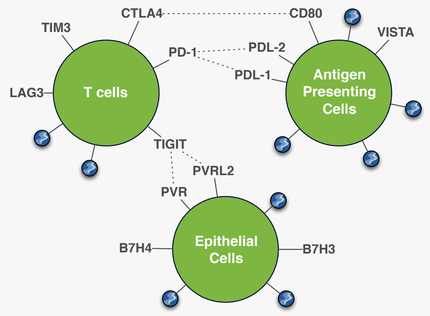
Target charcterization & prioritization
Based on patient derived molecular and clinical data



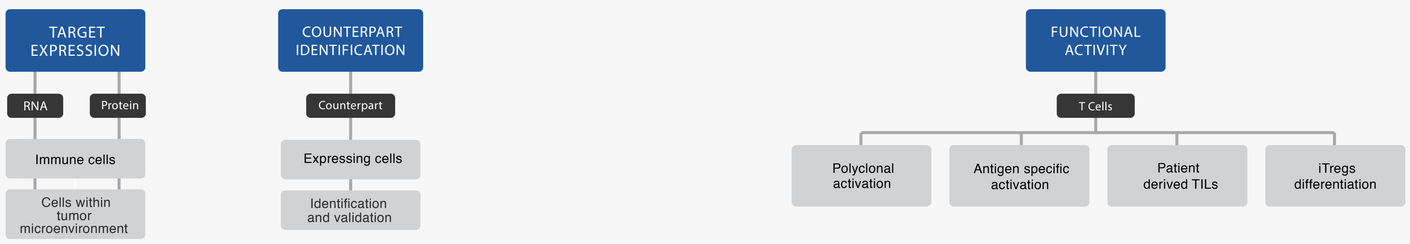
11277 Human Tumors
48 Tumor Types

3258 Normal Tissue Samples
30 Tissue Types

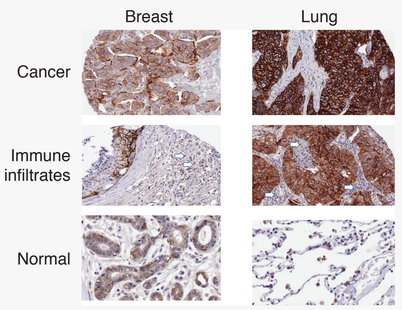
Diversified portfolio of immuno-oncology targets



Immune Checkpoint Experimental Validation

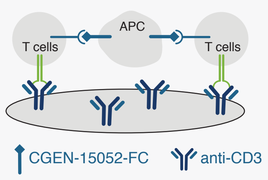


CGEN-15052 Protein Expression

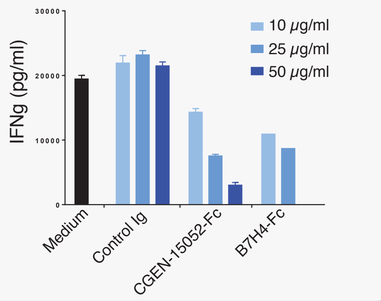


IHC staining using poly-clonal antibodies for CGEN-15052

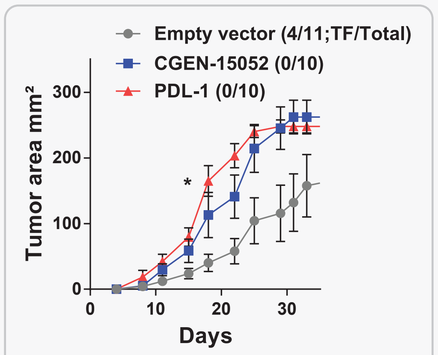
Soluble fusion protein comprised of the extra-cellular domain of CGEN-15052 inhibits anti-CD3 activated splenocytes



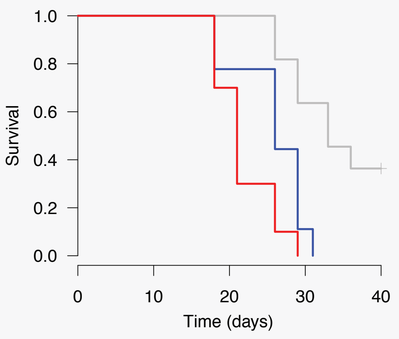
Soluble CGEN-15052-Fc Inhibits Mouse T Cell Activation



B16 melanoma cells manipulated to express CGEN-15052 or PDL1 exhibit enhanced in vivo growth when transplanted to C57BL/6 mice



*** CGEN-15052 vs EV p=0.0003**
*** PDL-1 vs EV p<0.0001**

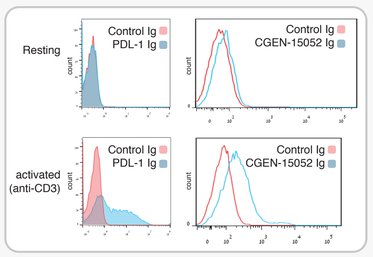


Log–rank P–value:
** CGEN-15052 vs EV P=0.0024
*** PDL1 vs EV P=7.4e-05

Excluding 4 TF mice in EV group:
**CGEN-15052 vs EV P=0.047
***PDL-1 vs EV P=0.0023

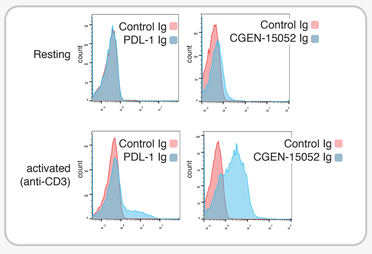
Counterpart Detection on activated T cells

Human CD4 T cells

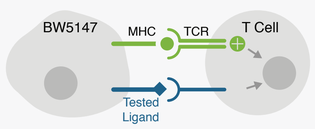


The fusion protein comprised of the extra-cellular domain of CGEN-15052 binds to primary CD4 and CD8 T cells in an activation dependent manner

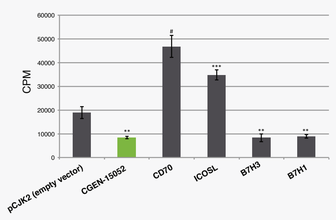
Human CD8 T cells



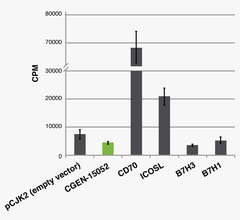
Expression of CGEN-15052 on BW1547 co-expressing membrane anti-CD3 results in reduced T cell activation



CD8⁺ T Cell Proliferation

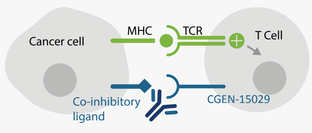


CD4⁺ T Cell Proliferation

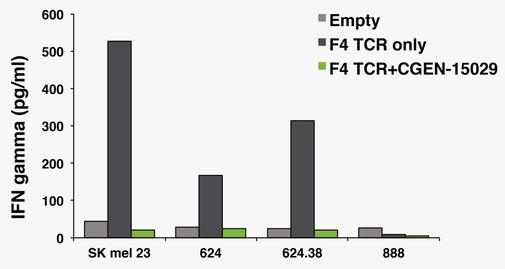


Steinberger & Leitner, University of Vienna

Forced co-expression of CGEN-15029 and F4 TCR (MART1 specific) on primary lymphocytes, inhibits antigen specific CD8 T cell activation in co-culture with melanoma cell lines



Inhibtion of CTL Activation



C. Cohen, Bar Ilan University, Israel