# 6. Bispecific Antibody addressing IL1RAP and CD3

**(City of Hope)**

5TH KDDF GLOBAL C&D TECH FAIR

## Asset Overview

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| **Product Type** | Antibody |
| **Disease Area** | Oncology |
| **Indication** | Acute Myeloid Leukemia (AML) |
| **Current Stage** | Discovery |
| **Target** | IL1RAP |
| **MoA** | Eliminate stem cells that drive AML and are responsible for remission |
| **Brief Description** | IL1RAP is a good target for immune therapy<br>• Interleukin-1 receptor accessory protein (IL1RAP, IL1R3) is a coreceptor involved in several signaling pathways including interleukin-1 (IL-1), IL-33, IL-36G, and stem cell factor (SCF).<br>• Signaling by IL-1 requires the formation of a cell surface receptor complex involving IL-1, interleukin-1 receptor type 1 (IL1R1), and IL1RAP. Lack of IL1RAP completely abrogates cellular responses to IL-1.<br>• IL1RAP is present on the cell surface of candidate chronic myeloid leukemia LSCs, AML blasts and CD34+ cells which include LSCs, and myelodysplastic syndrome, but not on normal HSC.<br>• Studies with IL1RAP-/- knockout mice indicate that IL1RAP is dispensable for normal HSC function. |
| **Intellectual Property** | WO2021030484A2 |
| **Publication** | - |
| **Inventors** | Bin Zhang, Weixu MENG, Guido Marcucci |

## Highlights

Expression of IL1RAP is specific for AML

- IL1RAP is highly upregulated in AML, especially in the CD34+ enriched fraction which includes LSCs. A mean of 97.5% CD34+ cells are IL1RAP+ in clinical samples (n=30). This level is comparable to CD123 and CD33 presently in clinical trial, and much higher than CLL1, another target against AML in clinical trial.
- In normal bone marrow, 14.7% CD34+ cells are IL1RAP+ much lower compared to 52.8% for CD123, 41.1% for CD33 and 48.4% for CLL-1. These antigens are being investigated for immune therapy of AML, and IL1RAP is expressed at significantly lower levels in normal HSCs than these. Thus, IL1RAP targeting is more selective.
- In CD34+ AML, IL1RAP expression is higher in cells in G0 phase of the cell cycle than those in G1 phase. This suggests IL1RAP will target quiescent AML blasts and LSCs.

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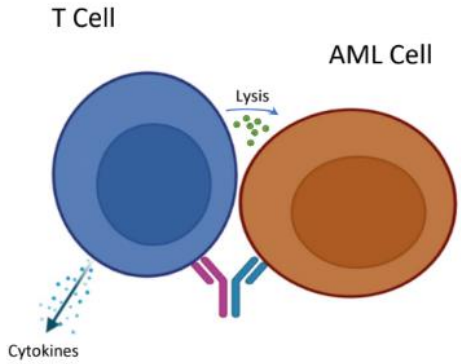
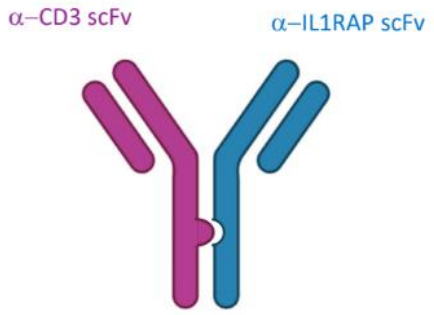
## Key Data

### Proof of Concept – IL1RAP Bispecific




Bispecific antibodies (BsAb) can bridge a tumor cell to a T cell, leading to an immunological synapse, T cell directed cytotoxicity and expanding the immune response.




Design: Knobs-into-holes design of bispecific using scFvs of Il1RAP and CD3.

### IL1RAP BsAb kills AML patient cells *in vitro* and *in vivo*