Specific treatment of Graft Versus Host Disease (GVHD) without affecting graft efficacy

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Technology description

Inhibition of Crk proteins specifically targets GVHD while not affecting graft versus leukemia

Market Need

Graft versus host disease (GVHD) can occur after an allogenic hematopoetic stem cell transplantation when the donor immune cells attack host tissue recognized as foreign. For oncology alone, allogenic stem cell therapeutics were an over five billion dollar market in the US and Europe combined. Of the estimated 50,000 hematopoetic stem cell transplants occurring annually, up to 70% of patients develop some degree of GVHD. The disease can manifest as rashes or dermatitis, hepatitis or jaundice, and even disrupted gastrointestinal tract function. The current first-line treatment is the steroid predinisone, to which only around 50% of patients have a solid response and for which secondary complications such as increased susceptibility to infection can arise with extended use. The next steps for those that do not respond well is usually an immunosuppressive therapy, but there is no standard of care. Thus, there is a need for a better more specific treatment for GVHD, especially for those unresponsive to steroid treatment.

Technology Overview

The Burkhardt lab has discovered a method to treat GVHD, by the inhibition of the Crk or CrkL proteins. The method is specific to treatment of GVHD while not affecting the function of the graft against cancer cells. Through knockout mouse studies, the Burkhardt group demonstrated proof of concept that Crk is required for effective T-cell migration to sites of inflammation, but importantly, not required for homing to lymphoid organs. Using donor T-cells with Crk or CrkL knocked out, they showed in vivo that GVHD was attenuated in a mouse model, while the effect of the donor T-cells against leukemia was unaffected. Additionally, the technology has the potential to be adaptable to different formats, ranging from inhibition by a small molecule or antibody, to gene-therapy means of Crk knockdown, shRNA or siRNA. Inhibition of Crk for GVHD may provide a treatment that has minimal side effects and also maintains efficacy of the graft.

Application area

- Treatment of GVHD
- Treatment of autoimmune or inflammatory diseases

Advantages

• Specific treatment for GVHD that does not affect graft efficacy
• Decreased side effects compared to extended steroid use

Institution

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