Office of Technology Licensing
Intellectual property newsletter
St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
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Translating basic research into clinical uses

Dario Campana, MD, PhD

Dr. Dario Campana developed a chimeric receptor and a cell expansion method in his laboratory that are on the verge of being used in St. Jude patients with acute lymphocytic leukemia (ALL). Chimeric receptors have been made and used by others, but Dr. Campana's laboratory discovered that the inclusion of the co-stimulatory factor 4-1BB markedly increases the activity of the receptor. The chimeric receptor currently being moved toward the clinic, anti CD19-BB-ζ, consists of a portion of a CD19 antibody as its extracellular domain, a hinge and transmembrane domain from CD8α and an internal 4-1BB signaling domain. This receptor binds to CD19, which is found on the surface of B-cell leukemias.

Dr. Campana's laboratory also discovered a technique for producing large, pure quantities of natural killer, NK, cells from a small amount of blood. This technique utilizes K562 cells modified to express large amounts of IL-15 and 4-1BB ligand on their cell surface. When a blood sample is placed on these K562-mb15-41BBL cells, the NK cells expand in numbers while other cell types, including T-cells, do not. An advantage to using NK cells to treat patients rather than T cells is the avoidance of graft versus host disease.

These two technologies are then combined. The CD19-BB-ζ chimeric receptor is put into the expanded NK cells obtained from a donor. These modified NK cells are then put into an immunosuppressed patient with ALL. The chimeric receptor directs the expanded NK cells to recognize, bind and destroy leukemia cells that express CD19 on their cell surface.

Dr. Campana, Dr. Leung and clinicians at St. Jude are developing a protocol to use this technology to treat St. Jude patients and hope to start recruiting candidates for this study by the summer of 2007.

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Attention investigators submitting grant applications to government agencies

Under the guidelines that now apply to all SF424 Grant Application submissions to U.S. government agencies, the OTL recommends that you begin to mark all information appearing in your applications that should be treated as confidential. This includes preliminary research results, original experimental designs and any other unpublished information that you feel should be treated as confidential. Particular attention should be paid to information that could lead to patentable subject matter.

If your SF424 application includes confidential information, the following statement should be included at the beginning of your research plan, whether it is the Introduction or Specific Aims:

> ***The following sections marked with an asterisk contain confidential unpublished information that [name of Applicant] requests not be released to person's outside of the Government, except for purposes of review and evaluation.**

All subsequent sections containing confidential information should be marked with an asterisk in the left hand margin. Information in your grant application that is not marked as indicated will be susceptible to public disclosure.

For the time being, the OTL will continue to also include its standard letter to help protect confidential information. Inclusion of this letter will be phased out for SF424 applications as the marking recommendation above is adopted since direct marking is considered to be a more effective form of protection. This letter will continue to be used for all non-SF424 grant applications

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What is prior art that destroys patentability?

Prior art is information disclosed to the public in any form before a given date that might be relevant to a patent's claims of originality. Examples of a public disclosure include:

- Publication in a journal
- Publication of an abstract
- Oral presentation
- Handout at a presentation
- Describing an invention on a web page
- Distributing preprints of an article
- Thesis
- Personal communication without a Confidentiality Agreement

An inventor can seek patent protection in the U.S. (and Canada in some circumstances) as long as a patent application is filed within one year of the first public disclosure of their invention. Outside the U.S., all patent rights are forfeited if the invention is publicly disclosed before an application is filed.

Consequences of not disclosing known prior art to the U.S. Patent Office

During the time an invention is being reviewed by the US Patent Office (USPTO), inventors and anyone involved in the filing and prosecution of a patent application have a duty to inform the USPTO of any prior art of which they are aware, whether it be from the inventor or another person. If this is not done and a patent eventually issues, it can be invalidated if it can be shown that anyone subject to this duty knew of prior art and intentionally withheld it.

The invention disclosure form used by St. Jude's OTL includes a question which alerts us to any prior art that the inventor(s) is aware of. Patent literature in the prior art is normally identified during the evaluation process by the OTL or during the patent drafting process by the patent attorney. However, inventors named on patent applications should be aware of the obligation to inform the USPTO if they know of or if during the patent office review of the application they become aware of any reference that might be relevant to the invention.

Pursuing your own invention: one person's experience

From time to time an employee will approach the Office of Technology Licensing (OTL) asking for advice about an invention they developed on their own at home independent of their affiliation with St. Jude. The OTL can provide some general guidance about how to obtain patent protection for these inventions, but does not have the authority or experience to do much beyond that. We have, however, run across an employee that can offer the benefit of her own personal experience chasing such a dream.

Meet Margaret Edwards. Margaret is a part time nurse at St. Jude and full time mother. In 1999, Margaret came up with the idea of making a bicycle seat for dolls for her daughter. When she found that no one sold such a thing, she recognized an opportunity and decided to go for it. Since that time Margaret has gone through the entire process of making and selling her doll bicycle seat, as well as patenting it along the way. It is currently sold under the name *Dolly Come Ride With Me*© through several internet outlets and specialty toy shops around the country. The process has been long and expensive thus far and it is not over yet. Although she has sold about 15,000 of her seats and has made it farther than most independent inventors, Margaret is still looking forward to the day when she has recovered her investment and begins to turn a profit.

If you have an idea of your own and would like to get a better understanding of what it really takes to turn it into a marketable product, we invite you to contact Margaret. She would also be interested in hearing from anyone who has ideas for marketing her seat. Margaret can be reached through contact information provided on her website at *www.dollycomeridewithme.com*.

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St. Jude's GMP facility is making a critical contribution to the effort to move this technology to the clinic. It will be making the CD19-BB-ζ chimeric receptor and expanding donor NK cells for clinical use. Without this facility this project would probably not be possible. Most pharmaceutical companies are unwilling to take the risk or make the investment needed to develop such an early stage product for a small patient population such as childhood leukemia. St. Jude's resources have created a unique opportunity to translate these two basic research discoveries into a clinical application.

The OTL filed patent applications on Dr. Campana's chimeric receptor in 2003 and his method for expanding NK cells in 2004. These applications are currently under review by the U.S. Patent Office. This technology has not been licensed, but companies are beginning to express interest. This interest is expected to increase as these ideas are tested in the clinic.