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UNIVERSITY  
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## **Autologous Cell-based Therapy for Autoimmune Diseases and Transplantation**

*Purification and use of CD14+ monocytes from Adult Blood to Induce Foxp3+ T-Regulatory cells in Adult Blood*

### **Contact**

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### **Inventors**

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### **Field**

Autoimmune disease  
Graft versus host disease (GvHD)

### **Technology**

Autologous cellular therapy

### **Key Features**

- Patient-specific treatment

### **Key Benefits**

- Autologous treatment
- Cellular therapy ready for immediate development
- Soluble factor available for follow up development

### **Stage of Development**

Cellular assays

### **Status**

Seeking development partner to commercialize this technology as a cellular therapy and to support continued research into the soluble factor(s) that are relevant to Treg induction

### **Patent Status**

US Application has been filed

### **Background**

Naturally occurring CD4+CD25+ regulatory T cells (Tregs) are crucial in immunoregulation and have great therapeutic potential for immunotherapy in the prevention of transplant rejection, allergy, and autoimmune diseases. Foxp3 functions as the master regulator in the development and function of Tregs, and there is evidence of Treg dysfunction in patients with autoimmune diseases like systemic lupus erythematosus. In animal studies, the induction or administration of Foxp3+ Tregs cells leads to significant reductions in disease severity in models of diabetes, multiple sclerosis, asthma, inflammatory bowel disease, thyroiditis and renal disease. These discoveries give hope that cellular therapies using Foxp3+ Tregs may help overcome these diseases in humans.

### **Current Treatments for Autoimmune Diseases**

Diseases of overactive immune function (both autoimmune and graft versus host disease) are treated with immunosuppressant drugs that inhibit various stages of immune function. Glucocorticoids are used to suppress cell-mediated immunity by inhibiting the interleukins. Antibodies to TNF- $\alpha$  function higher up in the inflammation signaling cascade. While these drugs have demonstrated efficacy, glucocorticoids have many undesirable side effects and TNF- $\alpha$  inhibition increases a patient's risk of opportunistic fungal infections.

### **Preferred Treatments**

Ideally, diseases resulting from low levels of Tregs would be treated by restoring Treg function - not managing the downstream consequences of aberrant immune function. Experimental models in mice have demonstrated that manipulating the numbers and/or function of Tregs can decrease pathology in a wide range of contexts, including transplantation and autoimmunity, and it is widely hoped that stimulation of Tregs in humans will be possible and useful.

One option is *in vivo* treatment with compounds that can induce Treg production, such as anti-CD3. Multiple groups have taken this approach and the use of anti-CD3 in clinical trials for various autoimmune diseases is ongoing. Another approach is induction of Treg production by treating a patient's blood *ex vivo*, expanding the Treg population in culture, and returning them to the patient by transplantation/injection.

### **Iwashima Invention**

Dr. Iwashima has developed a method for using CD14+ monocytes purified *from* adult peripheral blood to induce Treg production *in* peripheral blood. This unique method has been shown to be more potent than stimulation by umbilical cord blood or anti-CD3 stimulation, two other methods widely described in the scientific literature. Furthermore, it has been demonstrated that a soluble factor from the CD14+ monocytes induces the Foxp3 transformation. Thus, this technology is well positioned to enter the autoimmune disease market as a cellular therapy, with the potential for a follow up soluble drug (small molecule or protein) later, when the exact mechanisms by which CD14+ monocytes induce Treg production are elucidated.

