



TIRmed Pharma Publishes New Mechanistic Findings on TIR-01 in European Journal of Immunology

TIRmed Pharma, a biotechnology company developing next-generation treatments for autoimmune skin diseases, announces the publication of new research on its immunomodulatory oligonucleotide TIR-01 in the European Journal of Immunology. The study provides mechanistic insight into how TIR-01 affects human monocyte differentiation and supports the development of tolerogenic dendritic cells—processes that are central to immune regulation in inflammatory skin diseases such as atopic dermatitis (eczema).



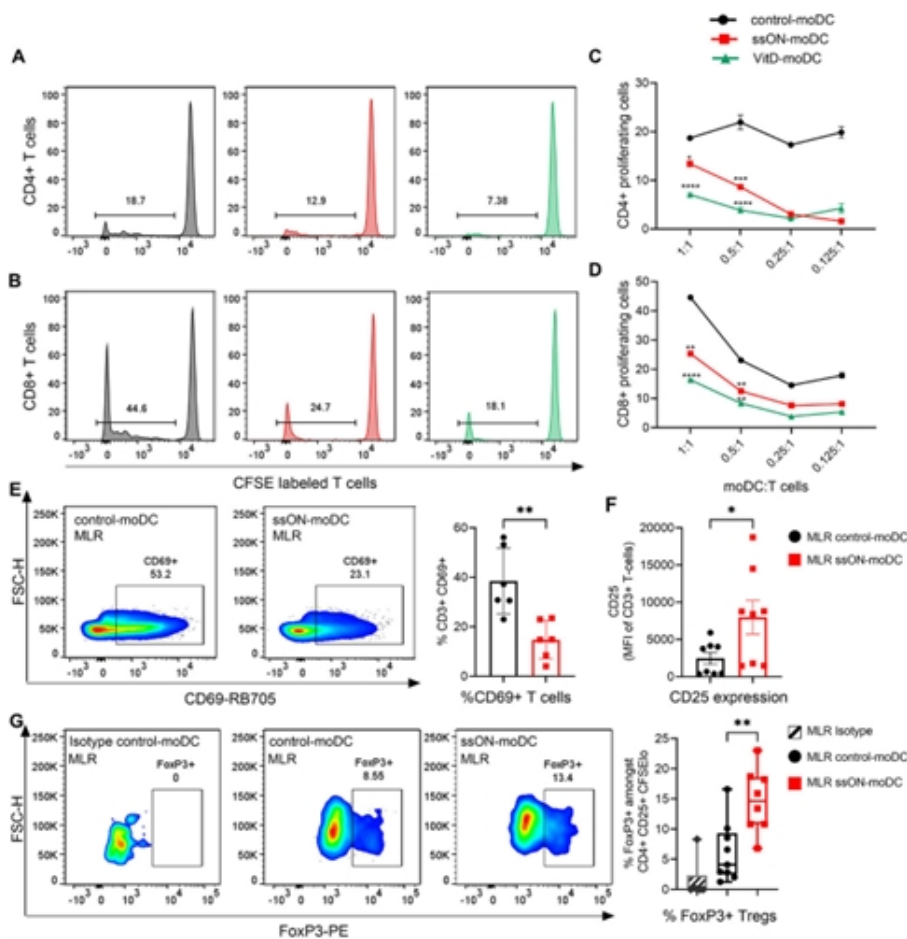
The work builds on earlier investigations of single-stranded noncoding oligonucleotides and their effects on immune regulation in vivo. In the present study, human monocytes were differentiated into dendritic cells in the presence of IL-4 and GM-CSF, with and without TIR-01 treatment.

The results show that the combination of IL-4, GM-CSF and TIR-01 generates dendritic cells with characteristics consistent with a tolerogenic phenotype. This includes both surface-marker expression and functional properties related to T-cell activation and regulatory T-cell induction.

These findings were supported by phenotypic, transcriptomic and functional analyses. Compared with untreated cells, TIR-01 influenced the differentiation process toward a more tolerogenic dendritic cell profile, reflected in altered surface-marker expression, a reduced capacity to activate T cells, and an increased induction of regulatory T cells. Gene-expression analyses further confirmed a shift toward immune-regulatory programming.

Key observations

- TIR-01 drives phenotypic changes associated with tolerogenic function, increasing PD-L1 expression while maintaining CD1a upregulation.
- Transcriptomic profiling showed that TIR-01 induced gene expression patterns that partly overlapped with Vitamin D-conditioned dendritic cells.
- The cells displayed altered responsiveness to lipopolysaccharide stimulation, indicating functional reprogramming.
- TIR-01 conditioned dendritic cells had a reduced capacity to stimulate alloreactive T cells in vitro.
- Instead, the cells supported the induction of CD4⁺FoxP3⁺CD25⁺ regulatory T cells.
- Chemical inhibition experiments suggest a role for PPAR-gamma in the differentiation process.



Representative data from the study published in the *European Journal of Immunology*.

Overall, the findings demonstrate that TIR-01's mechanism of action aligns with TIRmed's target profile. TIR-01 is the active substance in the company's topical treatment for atopic dermatitis and forms the basis for a new therapy based on similar immunomodulatory principles, with the aim of achieving durable control of skin inflammation.

"This publication provides important mechanistic insight into how TIR-01 interacts with early myeloid differentiation and promotes the development of tolerogenic dendritic cells. The data strengthen the scientific rationale behind our immunomodulatory strategy and support the continued advancement of our development program toward clinical studies," says Leo Holmgren, CEO of TIRmed Pharma.

About the study

The article, "Induction of Tolerogenic Dendritic Cells by a Noncoding Oligonucleotide," is published in the *European Journal of Immunology*. The research was conducted by teams at Stockholm University and Karolinska Institutet, led by Professor Anna-Lena Spetz, CSO and

co-founder of TIRmed Pharma. In academic publications, TIR-01 is referred to as ssON.

Full text (open access): <http://onlinelibrary.wiley.com/doi/10.1002/eji.70081>

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About TIRmed Pharma

TIRmed Pharma is a biotechnology company developing next-generation immunomodulatory therapies for autoimmune skin diseases, with an initial focus on atopic dermatitis (eczema). The company's drug candidate, TIR-C, is a topical oligonucleotide-based treatment that regulates immune responses and targets the disease's underlying mechanisms. Promising preclinical results support its potential to provide long-lasting relief and reduce treatment burden. Building on expertise in immunology and drug development, the company is pioneering new solutions in dermatological immunotherapy to enable more targeted and effective treatment options.

TIRmed Pharma is headquartered in Stockholm, Sweden. For more information, visit tirmedpharma.com and follow TIRmed on [LinkedIn](#).