ascenion Technology transfer for academic research
A company of the LifeScience Foundation

REFERENCE NUMBER TO 44-00014

UNCONVENTIONAL T CELL POPULATION AS BLOOD MARKER FOR CROHN'S DISEASE

Keywords: inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease (CD), T cell receptor (TCR), TCR repertoire, diagnosis, prognosis

INVENTION NOVELTY

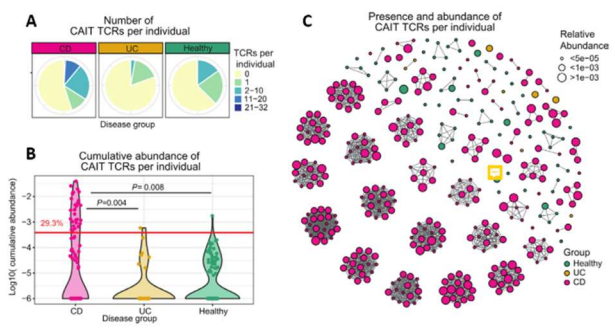
IBD refers to a chronic recurrent inflammation that can affect different parts of the gastrointestinal tract (UC: primarily colon; CD: entire GIT). The etiology of both subtypes (CD vs. UC) is not fully understood, but dysregulated T cell responses against intestinal antigens presented by environmental, dietary, or infectious agents have been found to be an important trigger. Given the general lack of knowledge, IBD can only be treated but not cured, and existing drugs are generally only effective for a subset of IBD patients. Furthermore, current treatments are prone to remission and/or the development of adverse effects. Accordingly, there is a high unmet medical need for appropriate biomarkers that can reliably distinguish the different subtypes of IBD, monitor treatment response, and serve as a potential target for drug development. The present technology discloses such a blood-based biomarker in the form of an unconventional population of CD-associated invariant T (CAIT) cells that are specific for CD and can distinguish it from other diseases of the GIT, i. e., UC and colorectal cancer (CRC).

VALUE PROPOSITION

IBD is a common (up to 1% in developed countries) and heterogenous disease, making it challenging to clearly determine the underlying disease causes, select the best therapy, and monitor treatment response and/or remission. Previous studies have identified distinct T cell receptor (TCR) traits and specific clonotypes, which are associated with the disease status and prognosis in individual patients. However, broader use of TCRs as disease biomarkers has not been possible due to high interindividual variability among patients. The invention discloses for the first time a semi-invariant family of TCR alpha motifs that have not been previously considered or studied in the context of IBD. The identified CAIT TCRs are highly enriched in the blood of CD patients and are subject to low interindividual variability as they are not dependent on classic human leukocyte antigens (HLAs) and can therefore be used to distinguish CD patients from UC patients or other diseases. It seems likely that CAIT TCRs can also be exploited as target for CD immunotherapy.

TECHNOLOGY DESCRIPTION

Based on a current hypothesis, proinflammatory immune responses in IBD are explained by dysregulated T cell reactions to yet unknown intestinal antigens. Accordingly, the inventors used high-throughput sequencing to profile the bulk TCR repertoires of both TCR alpha and beta chains in the peripheral blood of IBD patients and healthy controls (n=244). These studies led to the identification of a subgroup of clonotypes with semi-invariant TCR alpha chains that are markedly enriched in the blood of CD patients and expand in a population of CD8-positive T cells. To assess the presence and abundance of these CAIT TCRs in an independent cohort, matched samples of blood and intestinal tissue of patients with various GIT-associated diseases were examined. This latter cohort (n=37) consisted of patients with CD, UC, and CRC. In approximately two-thirds of CD patients, CAIT TCRs are significantly (>4-fold) overrepresented, accounting for more than 2.5% of the whole blood repertoire. In addition to diagnostic biomarkers, CAIT TCRs may also represent an interesting target for the treatment of CD.



Identification of CAIT alpha chains in blood. Proportion (A), Log-transformed cumulative abundance (B), and enrichment (C) of CAIT TCRs in patients by disease *(from Rosati et al. 2022)*.

DEVELOPMENT STATUS

The semi-invariant family of CAIT TCR alpha chains has been identified and validated in independent cohorts of patients. Further confirmational studies in a larger cohort (n=1,400) are currently under way. The same applies to investigations on the prognostic potential of these CD biomarkers.

COMMERCIAL OPPORTUNITY

The invention is available for co-development and in-licensing.

PATENT SITUATION

WO2023/118489A1 has been filed in December 2022.

FURTHER READING

Rosati *et al.*, 2022, Gut **71**: 2194; and Minervina et al., 2022 Gut.

Ascenion GmbH
Herzogstraße 64
D-80803 München
info@ascenion.de
www.ascenion.de

Licensing Contact
Dr. Torsten Stachelhaus
Technology Manager
T: +49 40 1888 43 48
stachelhaus@ascenion.de

Last updated Feb. 2024