Algorithms to Classify T Cell Activation by Autofluorescence Imaging

WARF: P190306US02

Inventors: Melissa Skala, Anthony Gitter, Zijie Wang, Alexandra Walsh

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a method to non-invasively detect T cell activation by imaging NAD(P)H. These algorithms can be applied to NAD(P)H images taken with commercial imaging flow cytometers/sorters, and fluorescence microscopes.

Overview

The importance of T cells in immunotherapy is driving the development of technologies to better characterize T cells and improve therapeutic efficacy. One specific objective is assessing antigen-induced T cell activation because only functionally active T cells are capable of killing the desired targets. Autofluorescence imaging can assess functional activity of individual T cells in a non-destructive manner by detecting endogenous changes in metabolic co-enzymes such as NAD(P)H. However, recognizing robust patterns of T cell activity is computationally challenging in the absence of exogenous labels or information-rich autofluorescence lifetime measurements.

Non-invasive, contrast-agent free determination of T cell behavior is imperative for advancing studies of T cells *in vivo* and for quality control of clinical adoptive immune transfer procedures (e.g., CAR T cell therapies).

The Invention

Building on award-winning work, UW–Madison researchers have discovered that autofluorescence intensity images of NAD(P)H can accurately classify T cells as activated or not activated ('naïve' or 'quiescent'), and have developed algorithms to classify T cell activation based on the images. Specifically, adapting pre-trained convolutional neural networks (CNNs) for the T cell activity classification task, T cells can be classified with 92 percent accuracy. These pre-trained CNNs perform better than classification based on summary statistics (e.g., cell size) or CNNs trained on the autofluorescence images alone.

This invention provides a way to non-invasively detect T cell activation by imaging NAD(P)H intensity. These algorithms can be applied to NAD(P)H images taken with commercial imaging flow cytometers / sorters, and fluorescence microscopes. If increased accuracy of T cell activation is needed for a specific application, additional measurements of the other NAD(P)H and FAD fluorescence endpoints can be obtained and used for classification.

Applications

- Screening and sorting activated T cells

Key Benefits

- Algorithms can be applied to existing commercial systems
- Method is non-invasive and contrast-agent free, hence can reduce reagent cost and variability
- Current methods to determine T cell activation require contrast agents and may require tissue/cell fixation

Stage of Development

The researchers have demonstrated that advanced machine learning models can accurately classify T cell activity from NAD(P)H intensity images and that those image-based signatures transfer across human donors.

Additional Information

Related Technologies

- WARF reference number P180292US02 describes a method and device to detect T cell activation by detection of autofluorescence from free NAD(P)H, or NAD(P)H α1. The device is also designed to allow sorting of T cells based on NAD(P)H α1.

Publications

- Wang Z. J., Walsh A. J., Skala M. C. and Gitter A. 2020. Classifying T Cell Activity in Autofluorescence Intensity Images with Convolutional Neural Networks. Journal of biophotonics, 13(3), e201960050.

Tech Fields

- Analytical Instrumentation : Microscopy
- Medical Devices : Diagnostics

For current licensing status, please contact Jeanine Burmania at jeanine@warf.org or 608-960-9846