



Algorithms to Classify T Cell Activation by Autofluorescence Imaging

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WARF: P190306US02

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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

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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

For More Information About the Inventors

- [Melissa Skala](#)
- [Anthony Gitter](#)

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 \$\alpha\$ 1. The device is also designed to allow sorting of T cells based on NAD\(P\)H \$\alpha\$ 1.](#)

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, Methods & Materials : Microscopy](#)
- [Medical Devices : Diagnostics & monitoring tools](#)

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