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Okun Lab

Help Us Advance Research: Participants Needed for Our Clinical Study In Israel

Every Mother Carries a Story. Some Stories Can Change Science.

Pregnancy creates a unique biological connection between mother and child, one that may leave traces for many years. In the Okun Laboratory at Bar-Ilan University, we are conducting a clinical study investigating whether biological signals exchanged during pregnancy may have lasting effects on a mother's health, with a particular focus on the relationship between **Down syndrome, pregnancy, and Alzheimer's disease**.

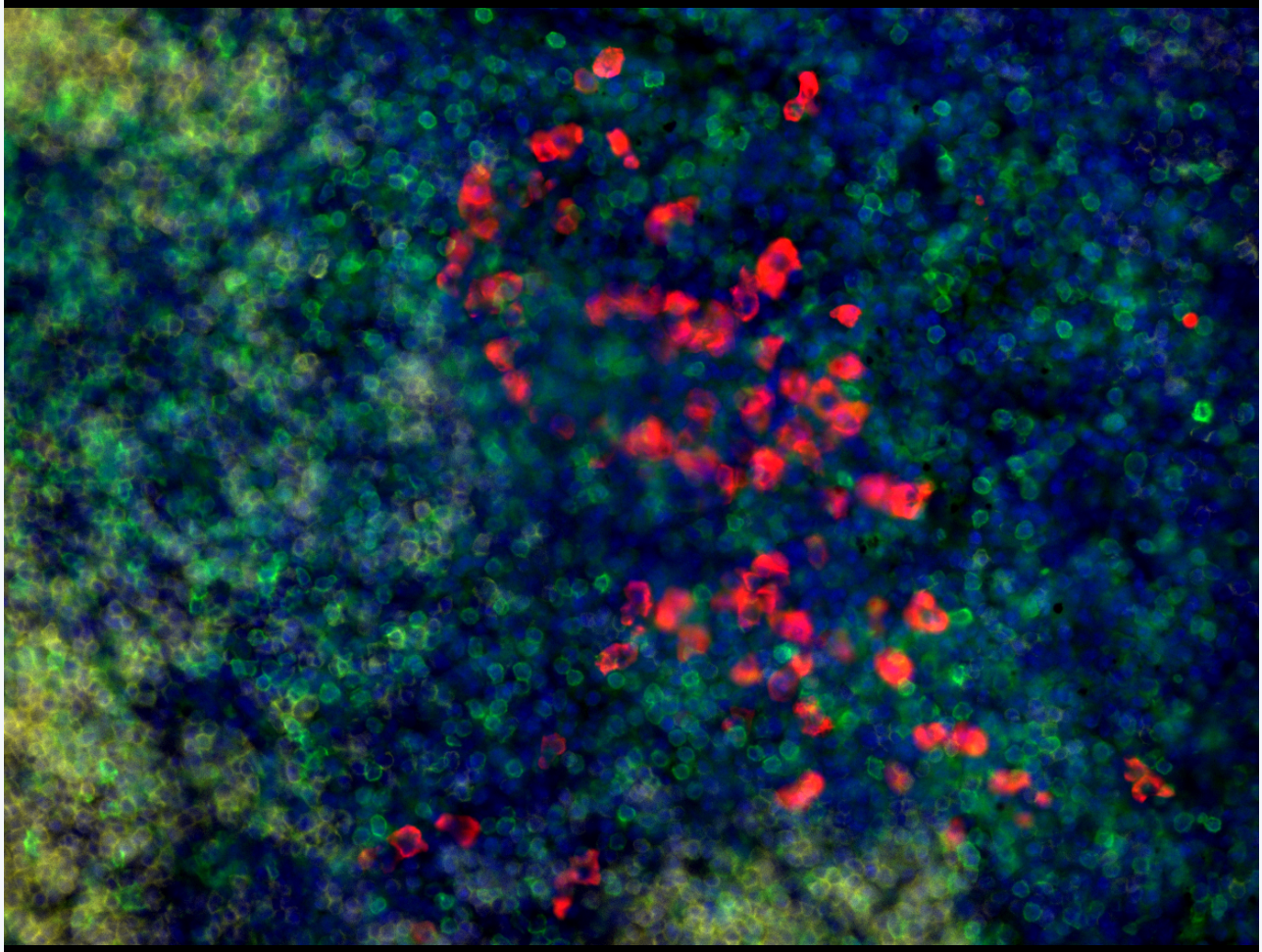
We are currently recruiting **women who are currently pregnant with a child with Down syndrome**, as well as **mothers of children with Down syndrome up to age 10**. Participation involves **a single blood sample and a brief medical and family history questionnaire**. Using advanced genetic, immunological, and molecular approaches, we hope to uncover biological mechanisms that have never before been studied in humans and, ultimately, contribute to a better understanding of women's brain health and Alzheimer's disease.

You can help even if you are not eligible to participate. If you know a family member, friend, colleague, physician, organization, or community that may be

relevant, we would greatly appreciate you sharing the study with them. Information about the study and the participation form are available through the Clinical Trial tab of our laboratory website.

Interested in participating or learning more?
Study information & registration — English
מידע על הצטרפות למחקר — עברית

Inside Our Research



Finding the Immune Cells That Are “Switched On”

At first glance, this image of the spleen looks like a dense sea of immune cells. Thousands of **T cells** and **B cells** occupy the tissue, each capable of responding to infection, tissue damage, and inflammatory signals. Yet only a very small fraction are actively engaging a particular immune pathway at any given moment. Those unique cells are highlighted here in **red.**

The red signal marks **phosphorylated IRF7 (p-IRF7)**. IRF7 is a key regulator of type I interferon response, one of the immune system's major pathways for sensing danger and coordinating inflammation. When IRF7 becomes phosphorylated, it is a sign that this signaling pathway has been activated. By staining for p-IRF7, we can therefore identify the relatively few immune cells that are actively responding among tens of thousands of surrounding cells.

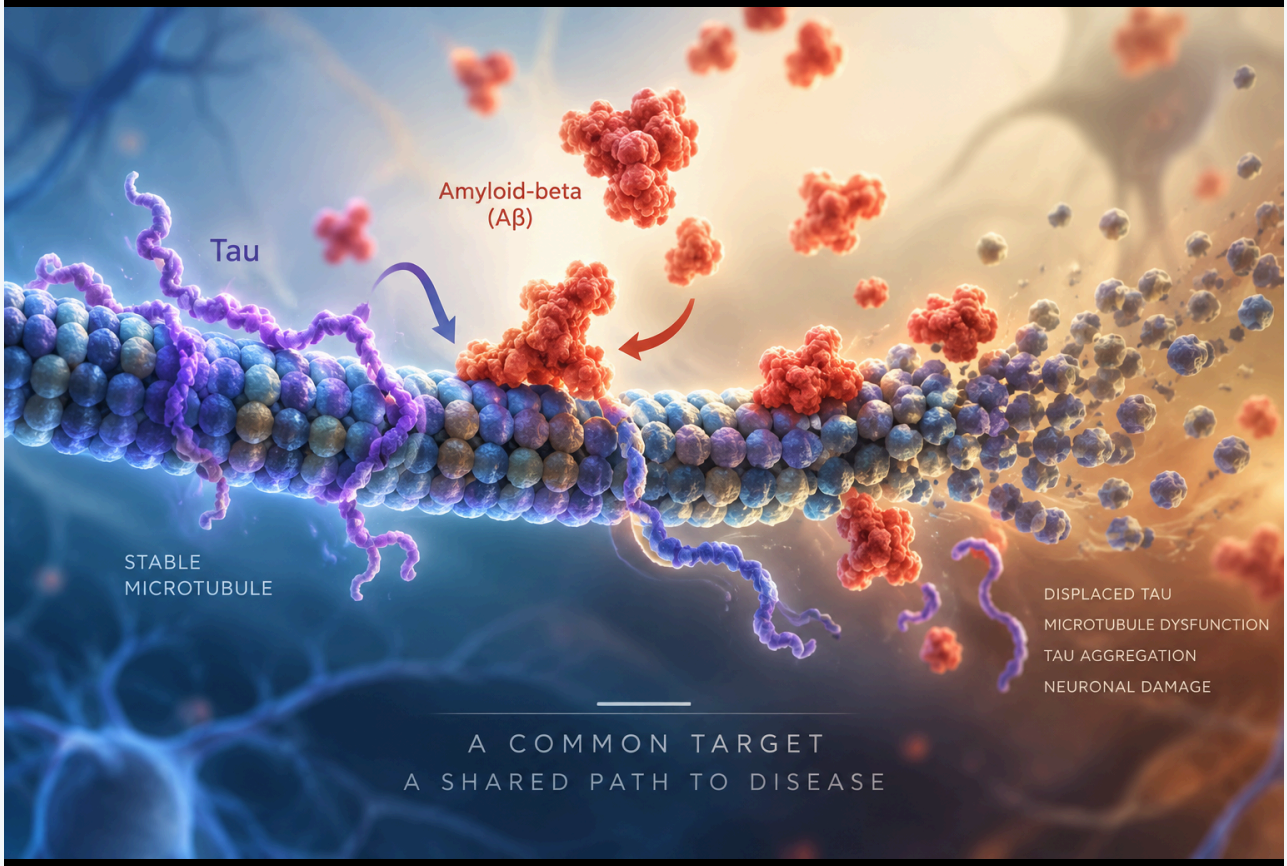
This becomes particularly important when we study **aging**. As we grow older, the immune system gradually shifts toward a state of persistent, low-grade inflammation, often referred to as **inflammaging**. At the same time, immune responses can become less precise: some inflammatory pathways become chronically activated, while protective responses may become weaker or poorly regulated.

By examining where p-IRF7-positive cells appear in the spleen, and whether they belong to specific B- or T-cell populations, we can begin to map which immune cells become abnormally active with age. We are especially interested in understanding whether persistent activation of interferon-related pathways contributes to the chronic inflammatory environment associated with aging.

Ultimately, these rare red cells may provide a window into a much larger process. By finding the small number of immune cells that are "switched on" within an entire tissue, we hope to understand how age-related immune activation develops, how it becomes sustained, and how it may contribute to declining tissue function and age-associated disease.

Image credit: Hadar Shtrasberg. Fluorescent imaging of activated immune cells expressing phosphorylated IRF7 (p-IRF7) within the mouse spleen. The Paul Feder Okun Laboratory for Alzheimer's Disease Research.

Highlights From The Field



What If Amyloid And Tau Are Competing For The Same "Railway Tracks"?

For decades, Alzheimer's disease research has revolved around two proteins: **amyloid-beta (Aβ)**, which accumulates in plaques outside

neurons, and **tau**, which forms tangles inside them. The problem is that these two hallmarks have never fit together neatly. Amyloid is strongly linked to inherited forms of Alzheimer's, yet tau pathology often tracks cognitive decline more closely. A new study in PNAS Nexus proposes a surprisingly simple way to connect the two.

Inside neurons, long structures called **microtubules** act like railway tracks, helping move essential materials up and down the cell. Tau normally binds to these tracks and helps regulate their function. The researchers found that amyloid-beta can also bind to microtubules, and with an affinity in the same general range as tau. In laboratory competition experiments, adding tau reduced amyloid-beta binding to microtubules, suggesting that the two proteins may compete for overlapping sites.

This leads to what the authors call the **"microtubule nexus" hypothesis**. Instead of amyloid plaques directly causing neuronal damage, soluble amyloid-beta inside neurons may begin the process by **pushing tau off microtubules**. Once displaced, tau is more prone to abnormal phosphorylation, mislocalization and aggregation, while the microtubules themselves become dysfunctional.

The model therefore creates a possible sequence: **too much amyloid-beta → tau displacement → microtubule failure → abnormal tau → neuronal damage.**

The idea is attractive because it may help explain a long-standing puzzle: why amyloid can be important early in the disease while **tau is more closely associated with neuronal dysfunction and cognitive decline.** It also suggests that plaques and tangles may partly be downstream signs of a deeper cellular problem, rather than the entire cause themselves.

There is an important caveat. This is still a **hypothesis**, supported here mainly by biochemical binding experiments with purified proteins and

stabilized microtubules. It remains to be shown that the same competition occurs inside living neurons and that it is strong enough to drive Alzheimer's disease. But if it does, it could shift attention toward a new therapeutic target: **protecting the microtubule-tau interaction before the familiar plaques and tangles appear.**

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