Cracking the code of chronic inflammation

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THE FRONT ROW at Scripps Research
FRONTROW.SCRIPPS.EDU
Increase knowledge  Help people
The Sundrud lab

Mission
Define mechanisms that cause chronic inflammation (increase knowledge) to design safer and more effective therapies (help people)

The Sundrud Lab @ Scripps FL
https://sundrudlab.com
What is Inflammation?

Celsius tetrad of inflammation (literally meaning “to set on fire”) - a.k.a., the 5 cardinal signs of inflammation

In today’s language:
Immune-mediated response to damaged or infected tissue

https://www.healthcoach7.com/2015/02/26/dna-carrying-inflammation/

http://dermaamin.com/site/images/clinical-pic/c/chilblain_lupus/

Inflammation – bad!

- Fatty Plaque
- Small Cell Lung Cancer (SCLC)
- Non-Small Cell Lung Cancer (NSCLC)

THE SECRET KILLER

- The surprising link between INFLAMMATION and HEART ATTACKS, CANCER, ALZHEIMER'S and other diseases
- What you can do to fight it

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at Scripps Research
1. Inflammation has enabled human evolution

2. Inflammation is the basis of vaccines
Inflammation is also the basis for cancer immunotherapy

Tasuku Honjo

James Allison

https://www.northshore.org/kellogg-cancer-center/our-services/immunotherapy/
Amin, JNCCN, 2020

Cancer cell

T cell

T cell approaches cancer cell.

T cell attacks cancer cell.

Cancer cell destroyed.
Current approaches to treating inflammation have consequences:

- **Inflammatory Bowel Disease**
- **Rheumatoid Arthritis**
- **Type 1 (Juvenile) Diabetes**
- **Psoriasis**

- Infections
- Cancers

[Image showing a close-up of a person's hand with rheumatoid arthritis, a vial labeled 'Remicade', a child with Type 1 Diabetes, and a person with psoriasis.]
How can inflammation be good and bad?

https://www.youtube.com/watch?v=TCxJFUzeQo
1. Inflammatory responses can be misdirected (Autoimmunity)

- Multiple Sclerosis
- Type 1 (Juvenile) Diabetes

https://www.news-medical.net/health/Anti-Myelin-Antibodies-in-Multiple-Sclerosis.aspx
https://medlineplus.gov/ency/article/000305.htm
2. Not all inflammatory responses are the same

<table>
<thead>
<tr>
<th>Type 1 responses</th>
<th>Type 2 responses</th>
<th>Type 3 responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracellular pathogens (e.g., viruses, intracellular bacteria)</td>
<td>Multicellular parasites (e.g., parasitic worms)</td>
<td>Extracellular bacteria, fungi</td>
</tr>
<tr>
<td>Macrophage, NK, CTL</td>
<td>Basophil, Eosinophil</td>
<td>Neutrophil, Epithelial repair</td>
</tr>
</tbody>
</table>

[Image of cell types and immune responses]
T cell activation determines the outcome of inflammation
Deciphering T cell dysfunction in chronic inflammation

Inflammatory Bowel Diseases (IBDs)

- Healthy
- Crohn's disease
- Ulcerative colitis

Environmental Factors
Genetic Predisposition
Gut Microbiota
Host Immune Response (Innate/Adaptive)

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at Scripps Research
T cells in the small intestine ‘adapt’ to bile acids
A precision medicine approach to treating Crohn’s disease

<table>
<thead>
<tr>
<th>Current SoC</th>
<th>BAS</th>
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<tbody>
<tr>
<td>Target:</td>
<td>Cause</td>
</tr>
<tr>
<td>Consequence</td>
<td></td>
</tr>
<tr>
<td>Mechanism of Action:</td>
<td>Local</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
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<tr>
<td>Immune suppression:</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Cost per dose:</td>
<td>$3.33</td>
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<td>$1,500</td>
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Increase knowledge  Help people
The Sundrud Lab: Probing the biology of T cells to treat the untreatable
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UPCOMING LECTURE

Mapping the Secret Complexity of Tumors to Defeat Aggressive Cancers

Michalina Janiszewska, PhD
Assistant Professor
Department of Molecular Medicine

Wednesday, April 21, 2021
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