

# RARE AUTOINFLAMMATORY DISEASES RESEARCH: SAVING LIVES, GIVING HOPE TO FAMILIES

Autoinflammatory diseases are a relatively new category of conditions that differ from autoimmune diseases. Although both kinds of illnesses happen when the immune system attacks the body's own tissues, they occur by different processes.

The NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), along with researchers from other parts of NIH and from around the globe, played a vital role in differentiating between the two groups of diseases, discovering the molecular causes for autoinflammatory diseases, and identifying and testing treatments. For more information about studies at the NIH for patients who have periodic fever syndromes or other autoinflammatory diseases, visit [http://niams.nih.gov/Research/Ongoing\\_Research/Branch\\_Lab/Clinical\\_Director/default.asp#fever](http://niams.nih.gov/Research/Ongoing_Research/Branch_Lab/Clinical_Director/default.asp#fever)

## THE INNATE AND ACQUIRED IMMUNE SYSTEM

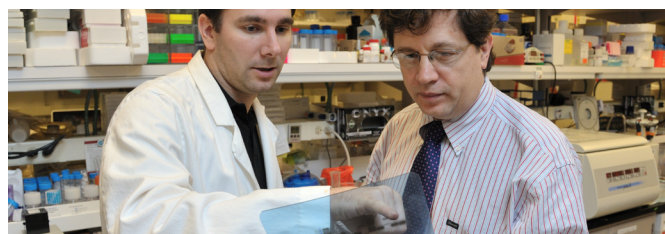
Your immune system defends you against infection. It has two parts: the acquired and the innate immune systems. The acquired (or adaptive) component develops over time. It produces antibodies that "remember" invaders and can fight them if they return. In autoimmune disease, antibodies and adaptive immune cells target the body's own healthy tissues by mistake. The more primitive innate (or inborn) immune system causes the heat, redness, and swelling that we associate with acute inflammation. In autoinflammatory diseases, the innate immune system reacts uncontrollably and for unknown reasons.

## AUTOINFLAMMATORY DISEASES: THEN AND NOW



### THEN (pre-1980s)

- The rarity of periodic fever diseases meant that even the most expert researchers would study only a few patients.
- Patients received medical care from their local doctors.
- Diseases were differentiated by symptoms or affected populations.
- Patients were treated with non-specific therapies such as steroids.
- Conditions affecting children often were fatal. Those who survived were left with severe disabilities.

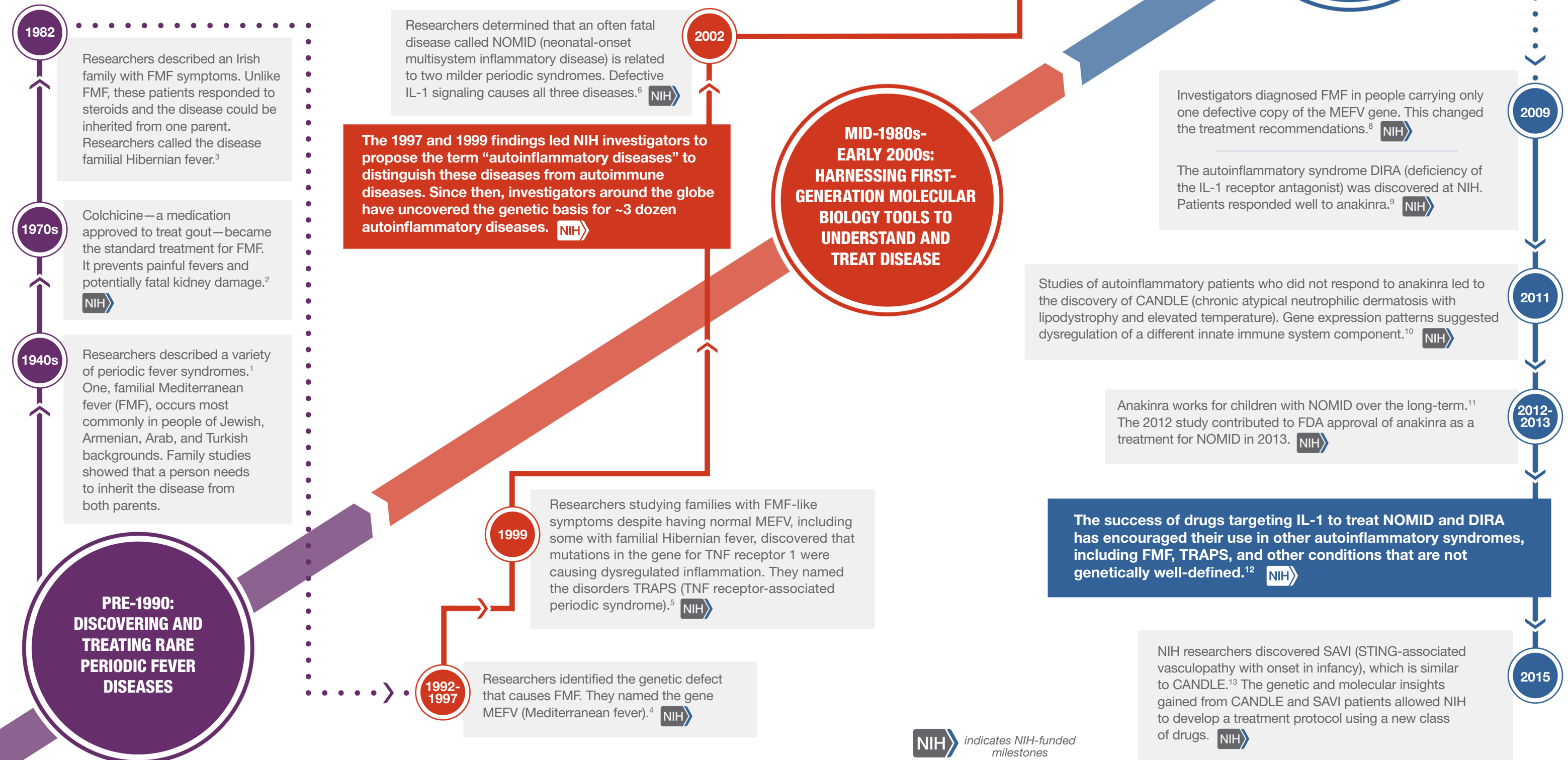


### NOW

- The global nature of research allows investigators to study many patients and make reliable conclusions about diseases.
- The NIH Clinical Center offers specialized care that patients from around the world can access.
- Genetic testing has revealed that many share common mechanisms.
- Treatments address the underlying molecular pathways that cause the symptoms.
- Early diagnosis and consistent treatment can prevent the devastating consequences of repeated episodes of inflammation.

# RESEARCH-TO-PRACTICE MILESTONES IN AUTOINFLAMMATORY DISEASES

For more information on the supporting evidence and research sponsors for these milestones, see the Web appendix.



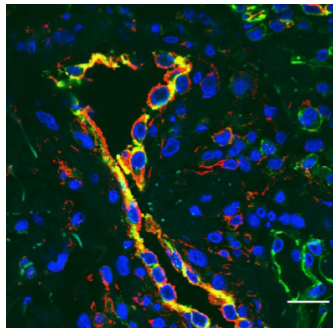
# IMPACTS OF STUDYING RARE AUTOINFLAMMATORY DISEASES

## KNOWLEDGE

- **Genetic studies of FMF and TRAPS defined a new class of diseases.**

By 2016, approximately 3 dozen autoinflammatory diseases had been identified.<sup>14</sup>

- **Studying autoinflammatory diseases revealed the inner workings of the innate immune system.**<sup>15</sup>
- **Rare autoinflammatory diseases are teaching us about the innate immune system's role in more common diseases.** For example, SAVI is providing insights about lupus.<sup>16</sup>



Blood vessels (outlined in yellow) of children with SAVI become inflamed, indicated here in red. Credit: Manfred Boehm, M.D., National Heart, Lung, and Blood Institute.

## HEALTH

- **An NIH study contributed to FDA approval of anakinra as the first treatment for NOMID.**<sup>17</sup> If left untreated, NOMID can lead to hearing and vision loss, cognitive impairment, physical disability, and death.
- **Anakinra benefits patients with DIRA.**<sup>18</sup>
- **NIH scientists discovered a link among hard-to-treat disorders characterized by inflammation and fat loss.**<sup>19</sup> Several drugs act on the molecular pathway that is altered in CANDLE and SAVI. Patients can enroll in a compassionate use trial at the NIH Clinical Center.

Understanding how autoinflammatory diseases are similar to and different from one another has led to life-saving and health-preserving treatments for people affected by these devastating diseases.



Caption: Alex, then and now, with Dr. Goldbach-Mansky. Credit: Kate Barton and Susan Bettendorf (NIH)

## MORE ABOUT CERTAIN AUTOINFLAMMATORY DISEASES

**FMF (Familial Mediterranean fever):** FMF occurs most commonly in people of Jewish, Armenian, Arab, and Turkish backgrounds; between 1 in 200 and 1 in 1,000 people in these populations have FMF.<sup>20</sup> Although colchicine helps, some people respond better to IL-1 inhibitors. This suggests that FMF is more complicated than previously thought.<sup>21</sup>

**TRAPS (TNF receptor-associated periodic syndrome):** TRAPS, which includes familial Hibernian fever, affects more than 1,000 people worldwide.<sup>22</sup> Symptoms resemble FMF, but TRAPS is caused by mutations in the gene for TNF receptor 1. Drugs that interfere with TNF sometimes help. Because some patients respond to drugs that affect IL-1 activity, NIH researchers are examining the link between defective TNF receptor 1 molecules and IL-1-mediated diseases.<sup>23</sup>

**NOMID (neonatal-onset multisystem inflammatory disease):** Fewer than 100 people worldwide have NOMID. 53 participated in the NIH-led trial that contributed to the FDA approval of anakinra as a treatment for NOMID.<sup>24</sup>

**DIRA (deficiency of the IL-1 receptor antagonist):** Although mutations that cause DIRA are rare, as many as 2.5 percent of people in northwest Puerto Rico are carriers; approximately 1 in 6,300 babies born in this region have DIRA. Mutations also are more common in individuals of Dutch descent. Anakinra is effective.

**CANDLE (chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature) and SAVI (STING-associated vasculopathy with onset in infancy):** Some children have defects in immune processes that are controlled by proteins called type 1 interferons. They may benefit from a compound that acts on interferon signaling.

Read more at [http://www.niams.nih.gov/Health\\_Info/Autoinflammatory/](http://www.niams.nih.gov/Health_Info/Autoinflammatory/)

For references, supplementary information, and more on the impact of NIH, please visit <http://www.nih.gov/impact>