INTRODUCTION

Inflammation's Yin-Yang

REDNESS, SWELLING, HEAT, PAIN. THESE WELL-KNOWN HALLMARKS OF INFLAMMATION were described over 2000 years ago by Celsus and are familiar to anyone who has gotten an infected cut or sprained their ankle. Fortunately, the symptoms of acute inflammation dissipate rapidly, and although inconvenient, they are also reassuring—they represent the immune system in action. The immune system clears the infection, guides the repair of damaged tissue, and the symptoms disappear.

Unfortunately, the very thing that is so beneficial during an infection can contribute substantially to the pathogenesis of several age-related chronic diseases such as metabolic disease/type 2 diabetes, cardiovascular disease, and neurodegenerative disease. In these diseases, saturated fatty acids, apolipoprotein B–containing lipoproteins, and the formation of protein aggregates, respectively, trigger activation of the immune system that results in inflammation. Thus, the immune system goes into overdrive. Because the stimulus that triggers the inflammation isn't easily cleared, it persists and contributes substantially to disease.

This special section in *Science* highlights the detrimental, but also in some cases beneficial, role of inflammation in neurodegenerative disease, cardiovascular disease, and metabolic syndrome. Aguzzi *et al.* (p. 156) focus on the role that microglia, resident macrophage-like cells in the brain, play in neurodegenerative diseases such as Alzheimer's disease, prion diseases, and traumatic brain injury. Although microglia can worsen disease, they are also important mediators of tissue repair and so also play protective roles in the brain. Swirski and Nahrendorf (p. 161) discuss the harmful and protective roles that leukocytes play in atherosclerosis and myocardial infarction. For instance, although leukocytes are important for tissue repair after a heart attack, their mobilization can worsen atherosclerotic plaques and lead to another infarction. Tabas and Glass (p. 166) use rheumatoid arthritis as a model to discuss how to develop therapies to target inflammation in cardiovascular disease. Finally, Odegaard and Chawla (p. 172) discuss how inflammation associated with obesity contributes to metabolic disease, but also point out the important role played by the immune system in maintaining an insulin-sensitive environment.

In *Science Signaling*, Research Resources by Warner *et al*. and auf dem Keller *et al*. highlight regulators of a receptor implicated in Crohn's disease (discussed in a Podcast with Gabriel Núñez) and the role of a matrix metalloproteinase in skin inflammation, respectively. A Perspective by Steinman discusses proinflammatory cytokines and diseases of the central nervous system, and a Perspective by Silke and Strasser focuses on the regulation of apoptosis and programmed necrosis in vivo.

These articles highlight the complicated roles that the immune system plays in chronic disease, suggest areas where more research and research tools are needed, and illuminate potential therapeutic strategies. Hopefully, careful manipulation of the immune system will add much-needed therapeutic tools to the arsenal to combat these already difficult-to-treat diseases. **– KRISTEN MUELLER**

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Science

Published by AAAS

Inflammation's Yin-Yang

Kristen Mueller

Science **339** (6116), 155.
DOI: 10.1126/science.339.6116.155