

Inflammatory mechanisms of atrial fibrillation

Basic Science Studies

Atrial Fibrillation Innovation Center

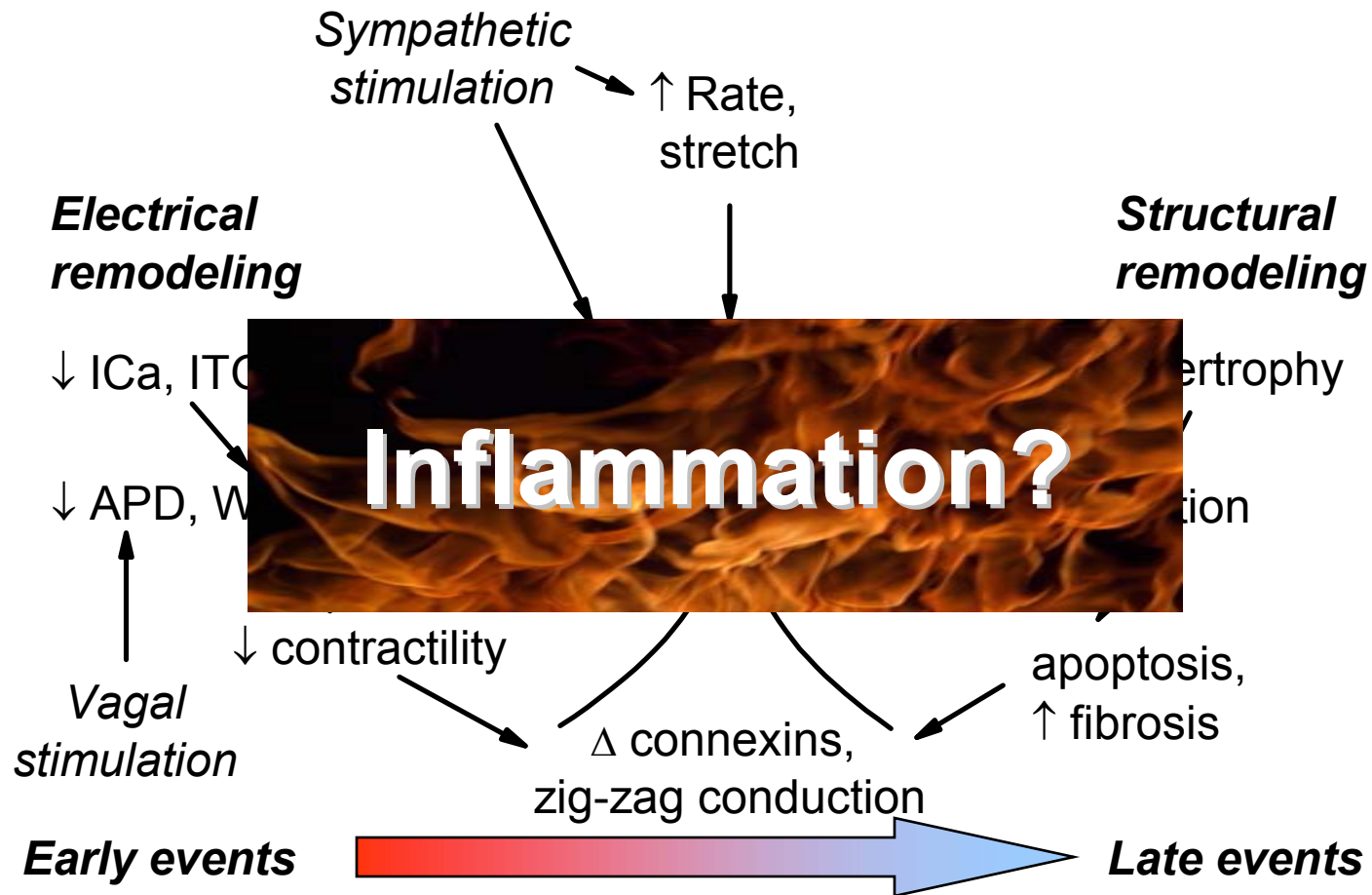
An Ohio Wright Center of Innovation



Ongoing basic science projects

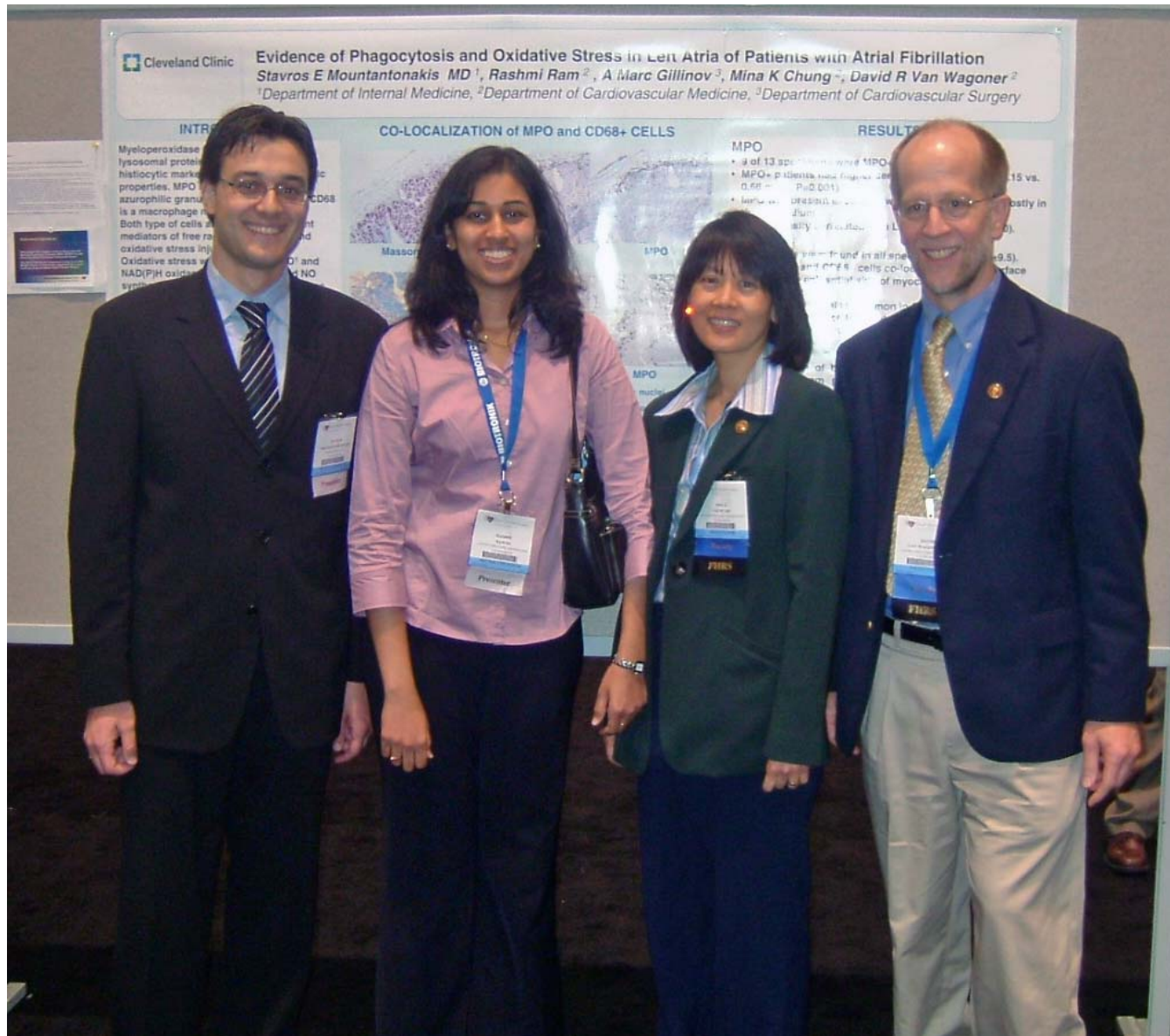
- **1) Human atrial histopathology**
- **2) Impact of AF on atrial connexins**
- **3) Microarray studies**
- **4) Post-surgical monitoring**
- **5) Lone AF – WGA analysis**
- **6) Complementary projects
(with alternative funding)**

Mechanisms of AF



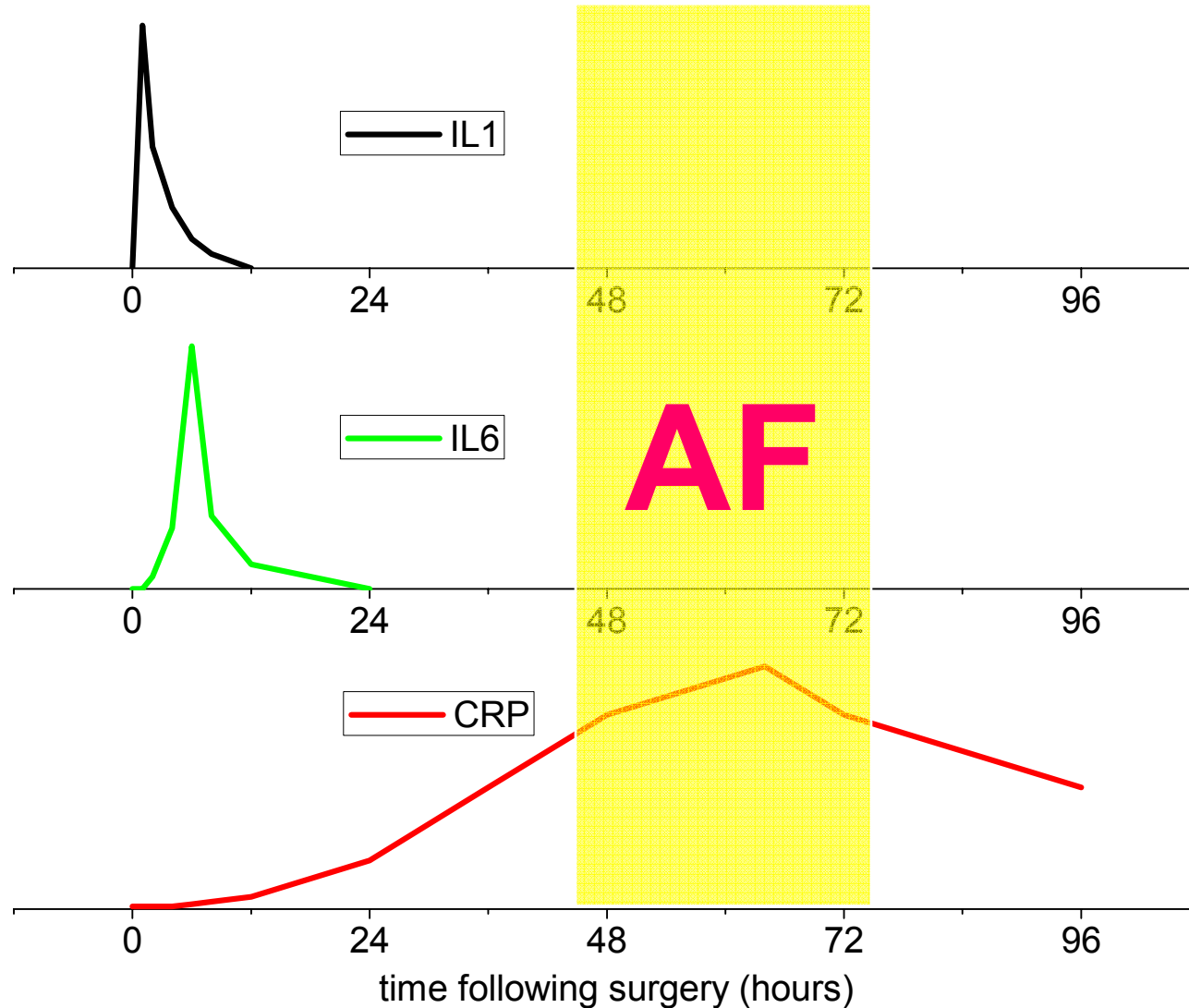
Project 1: Inflammation & atrial histology

- **Relationship between plasma markers of inflammation (CRP, MPO) and atrial histopathology in human AF**
- **Histologic impact of inflammatory mediators on atrial histopathology (C-reactive protein, CD3, CD68, myeloperoxidase staining)**
- **Clinical history analyzed for >400 AF surgery pts 2004-2006. >51 (17 / group x 3 groups) specimens w/ baseline CRP chosen for histology:**
 - **Control, h/o AF (SR at surgery), h/o AF (AF), lone AF;**
- **2 abstracts accepted and presented at Heart Rhythm 2006**



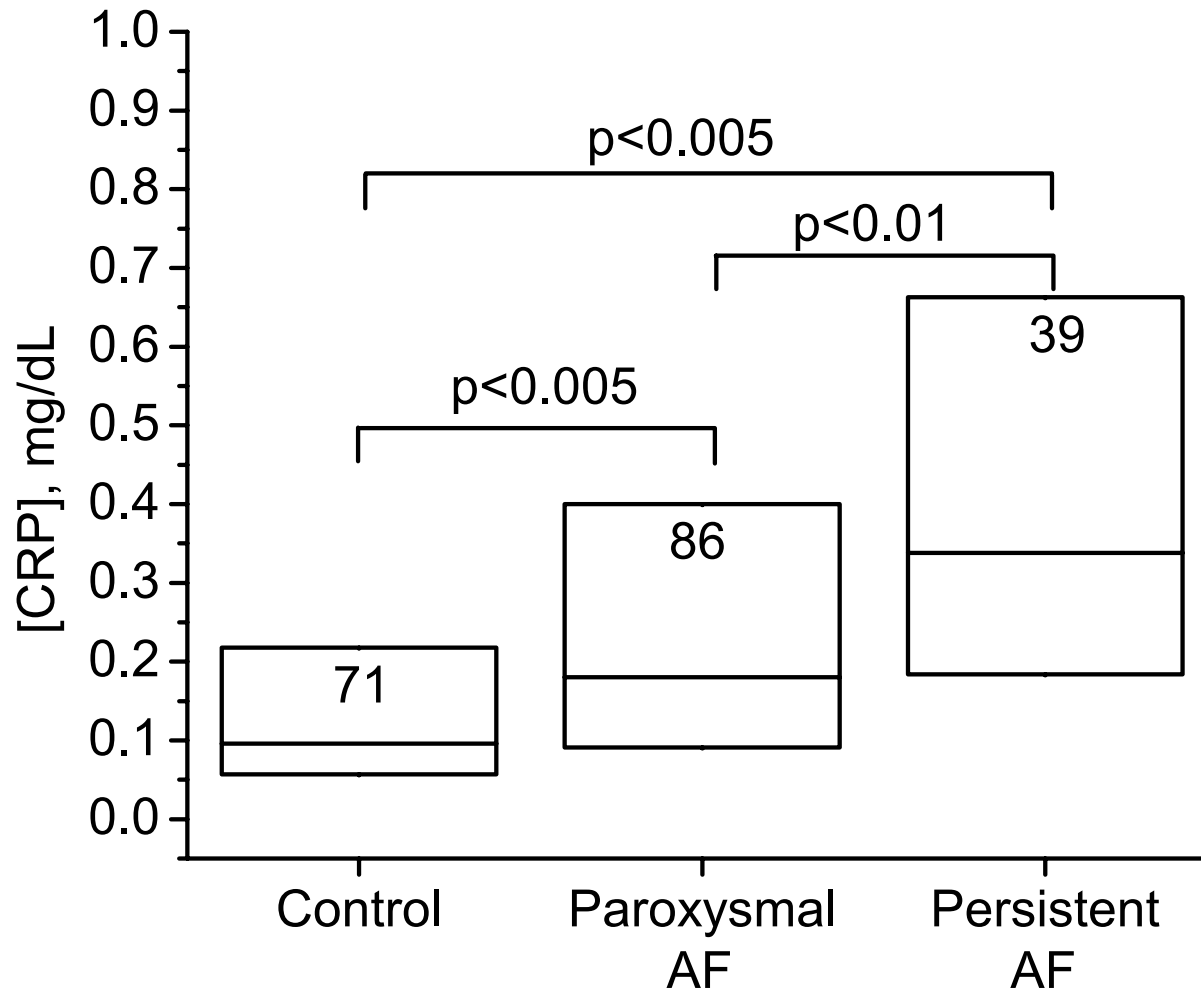
Stavros Mountantonakis, Rashmi Ram
Mina Chung, David Van Wagener

Cytokine changes following cardiac surgery



Adapted from: Bruins et al., *Circulation* 96:3542-3548, 1997

CRP is linked with arrhythmia persistence

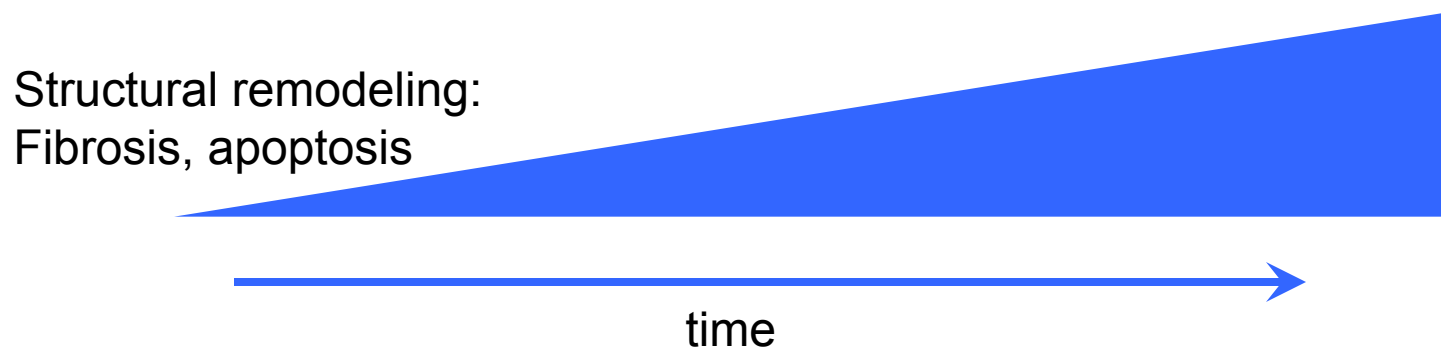


Mechanisms underlying AF persistence depend on comorbidities & AF duration

Brief episodes of AF, lone AF



Longer episodes of AF, aging, hypertension, heart failure



CRP binds to apoptotic cells: may act as an opsonin

C-reactive protein binds to both oxidized LDL and apoptotic cells through recognition of a common ligand: Phosphorylcholine of oxidized phospholipids

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Communicated by Daniel Steinberg, University of California at San Diego, La Jolla, CA, July 5, 2002 (received for review May 9, 2002)

C-reactive protein (CRP) is an acute-phase protein that binds specifically to phosphorylcholine (PC) as a component of microbial capsular polysaccharide and participates in the innate immune response against microorganisms. CRP elevation also is a major risk factor for cardiovascular disease. We previously demonstrated that EO6, an anti-oxidized LDL autoantibody, was a T15 clone-specific anti-PC antibody and specifically binds to PC on oxidized phosphatidylcholine (PtC) but not on native PtC. Similarly, EO6 binds apoptotic cells but not viable cells. In addition, such oxidized

mice. These antibodies, as exemplified by EO6, bind OxLDL but not native LDL (11). A subsequent characterization of EO6 revealed that it binds exclusively to oxidized PtC (OxPtC), such as POVPC [1-palmitoyl-2-(5-oxovaleroyl)-sn-glycero-3-phosphocholine] or to POVPC-protein adducts, but not to the native, nonoxidized PtC (12). Recent studies demonstrate that the PC headgroup is the obligatory moiety for EO6 binding (13). EO6 can block the binding and uptake of OxLDL by macrophage scavenger receptors, such as CD36 and SR-B1, as can its model

MK Chang et al., Proc Natl Acad Sci U S A.
2002 Oct 1;99(20):13043-8.