Rheumatoid arthritis and heart disease – surprisingly similar conditions

Helen Griffiths



An estimated
690,000 people
across the UK have
rheumatoid arthritis. That's
almost one in every hundred

31,000 new cases are diagnosed each year. **That's more than** three people every hour





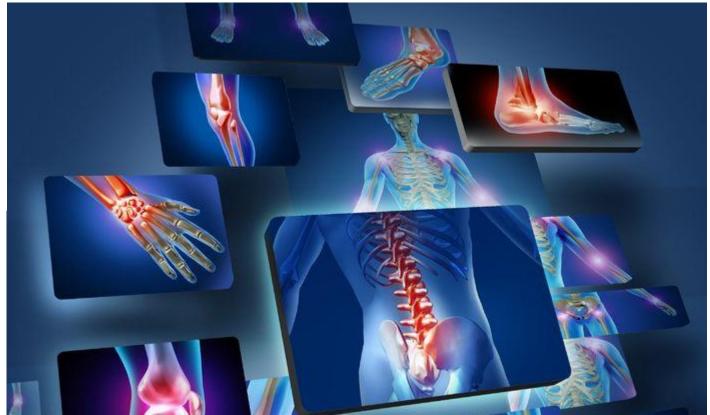
Onset most commonly occurs when people are in the prime of their working life or with a young family

Women are three times as likely as men to have RA





Rheumatoid arthritis



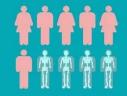
Vascular Disease is the collective term for diseases affecting the veins and arteries.



Vascular Disease is as common as **cancer**



Affects **4 million** people in the UK



Accounts for **40%** of deaths in the UK

What causes Vascular Disease?

Inflammation and weakness of the veins and arteries

Build-up of fatty deposits in the blood vessels



Symptoms and conditions include



PAD (Peripheral Arterial Disease)



High Blood Presure



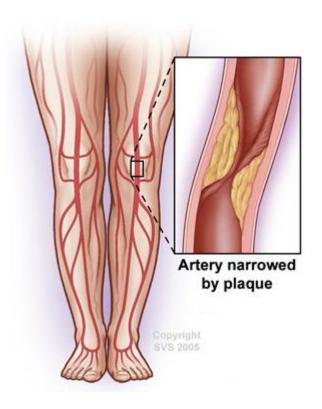
Heart Attack



Stroke



Heart/vascular disease



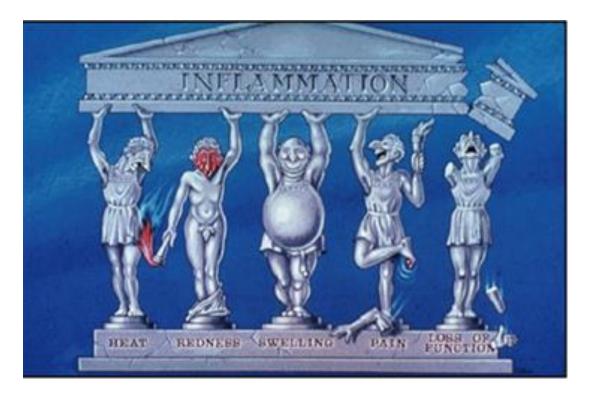
Shared environmental risk factors



Reactive oxygen species



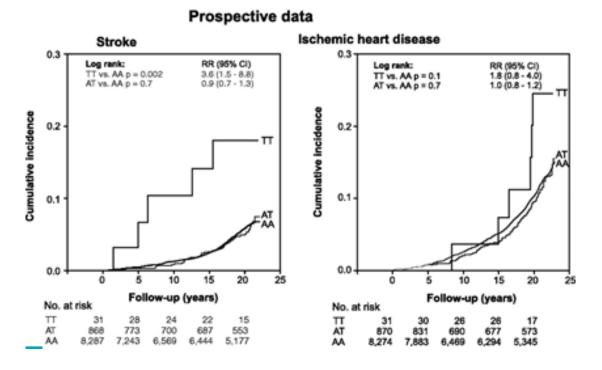
metabolism



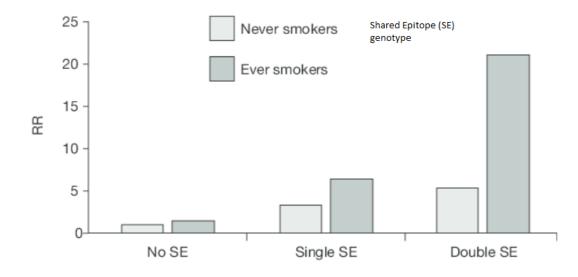
inflammation

Genetic risk factors for disease

Heart disease risk genes



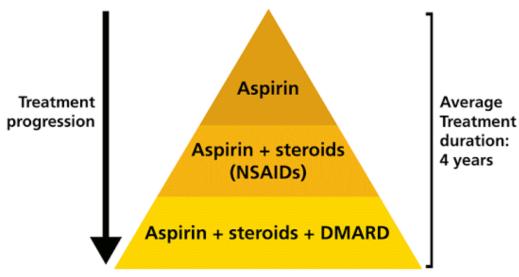
Arthritis risk factor genes



Apolipoprotein E Gene Polymorphisms Are Strong Predictors of Inflammation and Dyslipidemia in Rheumatoid Arthritis. The Journal of Rheumatology February 2012, 39 (2) 218-225

Rheumatoid arthritis and risk for heart disease

RA treatment pyramid: 1950's-1980's

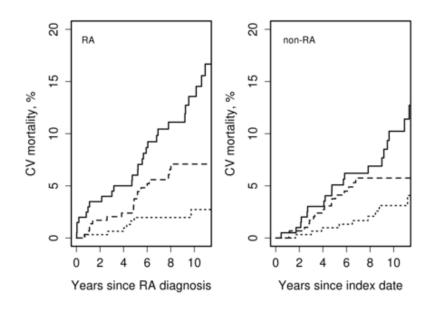


Rheumatology. Evolution of treatment for rheumatoid arthritis. Volume 51, Issue suppl 6. Sept. 14, 2012.

Toms TE, Panoulas VF, Douglas KMJ, et al
Statin use in rheumatoid arthritis in relation to actual cardiovascular risk: evidence for substantial undertreatment of lipid-associated cardiovascular risk?

Annals of the Rheumatic Diseases 2010;69:683-688.





Current treatments

Statins



Cholesterol Production
Blocked by Statin

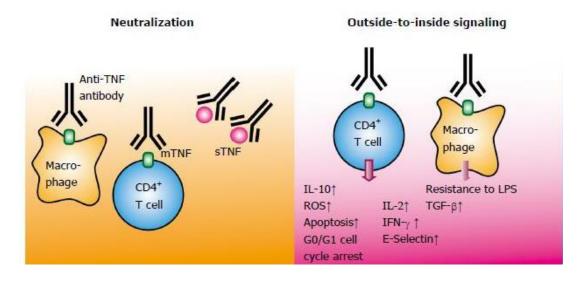
Cholesterol
HMG-CoA
Reductase

Targets lipid
metabolism

Anti-TNF drugs



Targets cell cross talk and inflammation



Not all patients can tolerate these drugs



Can we develop and use our knowledge of common pathways of disease to develop new treatments?



Our hypothesis - common pathways lead to poor outcomes

Metabolism

 Changes in lipid metabolism favour more inflammation and more reactive oxygen species production

Reactive oxygen specie

 Reactive oxygen species production is not timed well or delivered at the right time

Inflammation

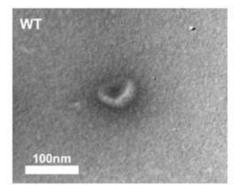
 Immune cells are less likely to die when and how they should

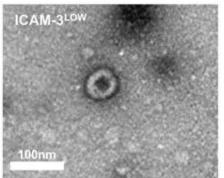
New disease management opportunities?

Lipid mediators to drive the resolution of

inflammation

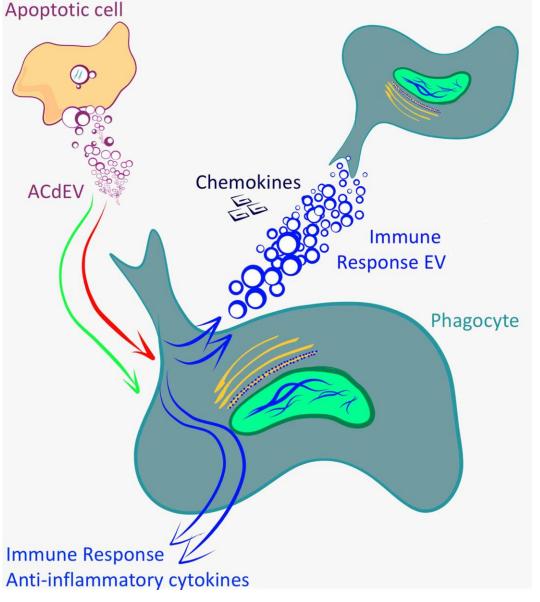
Devitt A, Griffiths HR, Milic I. 2018. Communicating with the dead: lipids, lipid mediators and extracellular vesicles. Biochem Soc Trans. 2018 May 9. pii:





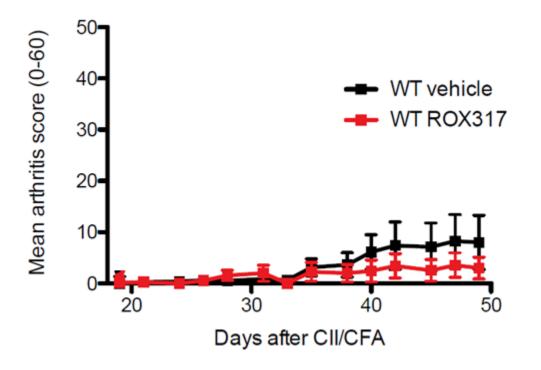


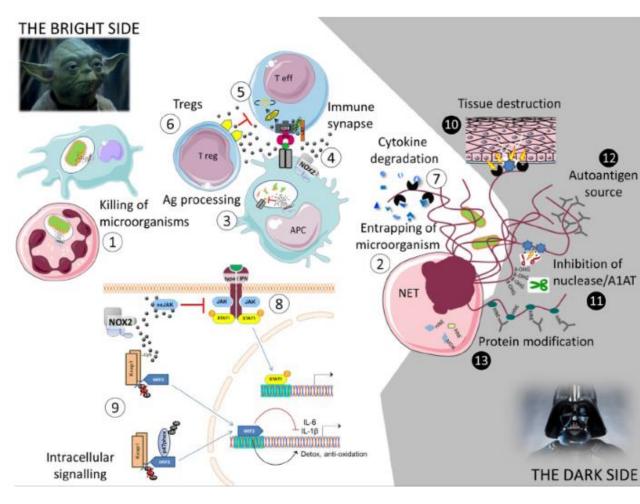




Controlled reactive oxygen species production

Hoffmann MH, Griffiths HR. The dual role of ROS in autoimmune and inflammatory diseases: Evidence from preclinical models. Free Radic Biol Med. 2018 Mar 15.





Concluding remarks

- A number of the chronic conditions that are seen as people get older have common underlying "aggravators"
- Inflammation is a common aggravator in arthritis and heart disease
- Our research aims is showing that we can manipulate lipid metabolism and reactive oxygen species production to reduce inflammation
- Preliminary experiments are showing this can be effective in treatment of long term conditions



Acknowledgments

- Andrew Devitt, Aston,
- Markus Hoffmann, Erlangen

- Malin Hultquist, Redoxis
- Paul Davies, Mologic

- Matt Rooney
- Isaac Ampong

Statin intervention study Aston University

Irundika Dias Caroline Brown

Lipid analysis Aston University

Ivana Milic Andrew Devitt Corinne Spickett Andy Pitt