

Professor Janet Lord BSc, PhD

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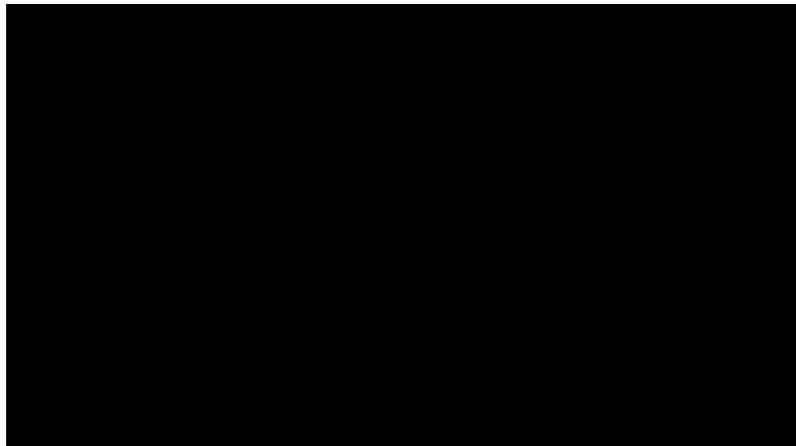
About

Janet Lord is director of the MRC-ARUK Centre for Musculoskeletal Ageing Research and the Medawar Centre for Healthy Ageing Research. She is also non-clinical lead for the University's Centre for Translational Inflammation Research located within the new Queen Elizabeth super Hospital which opened in the summer of 2011.

Janet's research focuses on the innate immune system, the body's front line defense against infection, and how the efficiency of this system is affected by ageing and stress, the latter including physical trauma and emotional stress such as bereavement. She is also interested in how the ageing of the immune system predisposes adults to chronic inflammatory diseases such as Rheumatoid Arthritis and COPD. In all of her work she aims to translate research findings into interventions, whether lifestyle (exercise, diet) or pharmacological, to improve immunity.

Janet Lord is also a leading member of the NIHR SRMRC, researching the impact of major trauma on the immune system and how this differs with age. Find out more about the work of the research centre on the [SRMRC website \(http://www.srmrc.nihr.ac.uk/\)](http://www.srmrc.nihr.ac.uk/).

Janet has published over 170 research papers in scientific journals as well as reviews and book chapters in the fields of immunosenescence, chronic inflammatory disease and neuroendocrine-immune biology. She was elected as a Fellow of the Academy of Medical Sciences in 2015 and awarded the Lord Cohen Medal by the British Society for Research into Ageing in 2013. Her research is currently funded by grants from MRC, Arthritis Research UK, AgeUK, NIHR, The Healing Foundation, the European Commission and the Glenn Foundation.



In this video Professor Janet Lord describes her career to date, her passion for her research and how it is helping to change the world, and how she enjoys working with postgraduate researchers from the UK and abroad.

Qualifications

- PhD Biological Sciences 1983
- BSc (Hons) Human Biology 1979

Biography

Janet Lord began her research career in the field of diabetes, gaining a PhD from the University of Aston in 1983 researching the link between obesity, diabetes and ageing. She went on to investigate signalling pathways involved in regulating insulin secretion, working with Steve Ashcroft at Oxford University, revealing the key role played by protein kinase C in this process. She returned to Birmingham and was awarded a Royal Society University Fellowship in 1989, allowing her to set up her own group looking at cell signalling in immune cells and its dysregulation in disease. She was promoted to the chair in immune cell biology in 2004.

She has made seminal contributions to the field of apoptosis, defining the PKC isoenzyme PKC-delta as an apoptotic lamin kinase and showing for the first time that the very short lifespan of neutrophils was due to their ability to activate death receptor signalling pathways in the absence of death receptor ligation. Her research has identified several novel therapeutic targets based upon the induction of apoptosis, most notably members of the PKC family.

In the last decade she has become interested in the effect of ageing and stress upon neutrophil function, including how innate immunity is regulated by the endocrine system. In 2010 she showed for the first time that the major adrenal steroid dehydroepiandrosterone sulphate was able to enhance neutrophil bactericidal function, revealing a biological function for this hormone distinct from its role as a precursor for the androgen DHEA. Her work suggests that a lack of this hormone in old age

results in older adults being more susceptible to the immune suppressive effects of the stress hormone cortisol after physical stress such as hip fracture or the emotional stress of a bereavement.

Professor Lord and her team now focus upon characterising signaling pathways that regulate innate immune cell function, with a special interest in the bactericidal processes and survival of neutrophils. This knowledge is used to develop novel therapies in three main areas; Immune senescence (loss of immune function with ageing), chronic inflammatory disease (Rheumatoid Arthritis) and Acute Myeloid Leukaemia.

Teaching

Teaching Programmes

- [Biomedical Science BSc \(/undergraduate/courses/med/biomedical-science.aspx\)](/undergraduate/courses/med/biomedical-science.aspx)
- [Medicine and Surgery MBChB \(/undergraduate/courses/med/medicine.aspx\)](/undergraduate/courses/med/medicine.aspx)
- [Clinical Health Research MRes \(/postgraduate/courses/combined/med/clinical-health-research.aspx\)](/postgraduate/courses/combined/med/clinical-health-research.aspx)
- [Musculoskeletal Ageing and Health MSc/PGDip \(/postgraduate/courses/taught/med/musculoskeletal-ageing.aspx\)](/postgraduate/courses/taught/med/musculoskeletal-ageing.aspx)

Postgraduate supervision

Janet supervises doctoral research students in the following areas:

- The mechanisms underlying reduced neutrophil function in ageing.
- Lifestyle factors (exercise, diet, sleep) influencing immune function in old age
- Stress and Immunity

If you are interesting in studying any of these subject areas please contact Janet on the contact details above, or for any general doctoral research enquiries, please email: dr@contacts.bham.ac.uk (<mailto:dr@contacts.bham.ac.uk>) or call +44 (0)121 414 5005.

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Research

RESEARCH THEMES

The effect of ageing on immunity; chronic inflammation; trauma; stress and immunity

RESEARCH ACTIVITY

Immune senescence and frailty

As humans age they become more susceptible to infectious diseases (especially bacterial infections), inflammatory disease, autoimmune disease and have poorer responses to vaccinations. Although ageing is a complex process, these data suggest that immune function may be reduced during ageing and will contribute to the increased morbidity of the elderly. Professor Lord's team has shown that neutrophil function declines with age, specifically that neutrophil phagocytosis of bacteria is reduced by almost half and also that neutrophil migration accuracy is reduced. The latter is important as inefficient migration leads to excess tissue damage as the cell migrates towards a site of infection and this may explain why older people are frailer after infection. The team are now testing interventions to improve neutrophil migration and reduce mortality in patients with pneumonia.

Prof Lord's studies also aim to determine if stress accelerates this loss of neutrophil function and makes the elderly more susceptible to infection and physical frailty. The research so far has shown that after hip-fracture or bereavement, the loss of neutrophil function is dramatically increased and almost half of hip fracture patients succumbed to serious bacterial infections. Importantly this work has revealed that this may be mediated by an excess of the immune suppressive stress hormone cortisol and a lack of the immune enhancing counter stress hormone dehydroepiandrosterone (DHEA). A raised cortisol:DHEAS ratio was also associated with poor physical function (frailty) up to 6 months after hip fracture. Professor Lord is now seeking funding to try and supplement hip fracture patients with DHEA to see if the number of infections in these patients can be reduced.

More recently the team associated with the MRC-ARUK Centre for Musculoskeletal Ageing Research have been studying older adults who have been physically very active all of their lives to determine how much of physical and immune ageing is due to increased inactivity with old age. So far this research has revealed that sarcopenia did not occur in these adults, but other aspects of ageing such as a decline in lung function did. The team are now examining immune function in these adults.

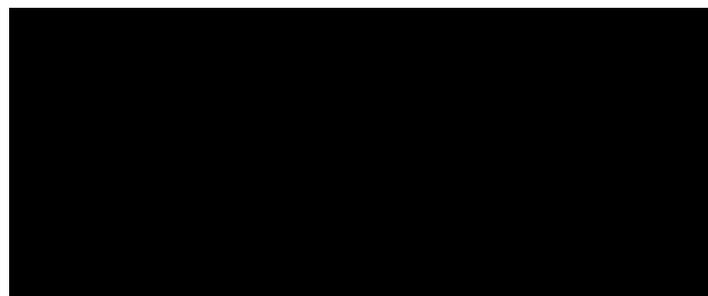
Chronic inflammatory disease

During an immune response inflammatory cells, including T cells and neutrophils, are recruited to sites of infection to help to clear pathogens. Once the site is rendered sterile these same cells must be removed efficiently to avoid non-specific attacks on healthy tissue. This is achieved in part by their death by apoptosis and removal by macrophages. Professor Lord and colleagues has shown that this process is dysregulated in chronic inflammatory diseases such as Rheumatoid arthritis, leading to the accumulation of inflammatory cells and destruction of healthy tissue by cells such as neutrophils. The group has identified signals from stromally derived cytokines (type 1 Interferon and GM-CSF) as regulators of neutrophil survival and stromal fibroblasts are now recognised as rational targets in rheumatoid arthritis.

This work has now progressed to consider the role of immunosenescence in the development of RA. Previous work by researchers in the US has shown that patients with established RA show features of accelerated immune ageing and Prof Lord has revealed that regulatory B cells, which play a role in preventing autoimmunity, are reduced with age. The team are now working with Prof Karim Raza to determine if immunosenescence appears in the very earliest stages of RA and could be a driver of pathology rather than a consequence.

Trauma

Major trauma is accompanied by a significant systemic inflammatory response (SIRS) accompanied by a compensatory anti-inflammatory response (CARS), however there is also major immunoparesis which leaves the patient at risk of infections and sepsis. In addition, both the endocrine (increased cortisol:DHEAS ratio) and inflammatory response promote a catabolic response which combined with immobility leads to dramatic loss of muscle. For the elderly patient that presents problems as the ability to restore muscle mass and strength is compromised with age. Prof Lords team in the SRMRC are following the inflammatory and endocrine response to trauma in young and elderly patients with the aim to develop intervention to improve immunity and reduce muscle loss and frailty after trauma.



Other activities

- Section editor for the journal *Aging Cell*

Publications

Hazeldine J, Hampson P, Opoku FA, Foster M, Lord JM (2015). *N*-formyl peptides drive mitochondrial damage associated molecular pattern induced neutrophil activation through ERK1/2 and P38 MAP Kinase signalling pathways. *Injury* 46:975-984.

Pollock RD, Carter S, Velloso CP, Duggal NA, Lord JM, Lazarus NR, Harridge SR (2015) An investigation into the relationship between age and physiological function in highly active older adults. *J Physiol* 593:657-680.

LordJM, MidwinterMJ, BelliA, BrohiK, KovacsEJ, KoendermanL, KubesP, ChenY-F, LilfordRJ (2014) The systemic immune response to trauma: an overview of pathophysiology and treatment. *Lancet* 384:1455-1465.

Hazeldine J, Hampson P, Lord JM (2014) The impact of trauma on neutrophil function. *Injury* doi:10.1016/j.injury.2014.06.021 (<http://dx.doi.org.ezproxyd.bham.ac.uk/10.1016/j.injury.2014.06.021>).

Sapey E, Greenwood H, Walton G, Mann E, Love A, Aaronson N, Insall RH, Stockley RA, Lord JM (2014) Phosphoinositide 3 kinase inhibition restores neutrophil accuracy in the elderly: towards targeted treatments for immunosenescence. *Blood* 123:239-248.

Baylis D, Ntani G, Edwards MH, Syddall HE, Bartlett DB, Dennison EM, Martin-Ruiz C, von Zglinicki T, Kuh D, Lord JM, Sayer AA, Cooper CF (2014) Inflammation, telomere length and grip strength: a 10 year longitudinal study. *Calcified Tissue Int* 95:54-63.

Duggal NA, Upton JA, Phillips AC, Sapey E, Lord JM (2013) An age-related numerical and functional deficit in CD19⁺CD24^{hi}CD38^{hi} B cells is associated with an increase in systemic autoimmunity. *Aging Cell* 12:873-881.

Duggal NA, Upton JA, Phillips AC, Hampson P, Lord JM (2013). Depressive symptoms are associated with reduced neutrophil superoxide generation in hip fracture patients. *Brain Behavior Immunity* 33:173-182.

Phillips AC, Upton JA, Duggal NA, Carroll D, Lord JM (2013). New onset depression following hip fracture is associated with increased physical frailty in older adults: the role of the cortisol:dehydroepiandrosterone sulphate ratio. *BMC Geriatrics* 13:60.

Hazeldine J, Hampson P, Lord JM (2012) Reduced release and binding of perforin at the immunological synapse underlies the age-related decline in Natural Killer cell cytotoxicity. *Aging Cell* 11:751-759.

Bartlett DB, Firth CM, Phillips AC, Moss P, Baylis D, Syddall H, Sayer AA, Cooper C, Lord JM (2012). The age-related increase in low grade systemic inflammation (Inflammaging) is not driven by cytomegalovirus infection. *Aging Cell* 11:912-915.

Baylis D, Bartlett DB, Syddall HE, Ntani G, Gale CR, Cooper C, Lord JM, Sayer AA (2013) Immune-endocrine biomarkers as predictors of frailty and mortality: a ten year longitudinal study in community dwelling older people *AGE* 35:963-971.

Jansen JO, Lord JM, Thickett D, Midwinter MJ, McAuley DF and Gao F (2013). Statins and Trauma: a systematic review. *Crit Care* 17:227.

Wang K, Hampson P, Hazeldine J, Kryštof V, Strnad M, Pechan P, Lord JM (2012) Cyclin-Dependent Kinase 9 activity regulates neutrophil spontaneous apoptosis. *PLoS ONE* 7(1): e30128. doi:10.1371/journal.pone.0030128.

Khanfer R, Lord JM, Phillips AC (2011) Neutrophil function and cortisol:DHEAS ratio in bereaved older adults. *Brain Behavior and Immunity*. 25:1182-1186.

Radford DJ, Wang K, McNelis JC, Taylor AE, Hechenberger G, Hofmann J, Chahal H, Arlt W and Lord JM (2010) Dehydroepiandrosterone sulfate directly activates protein kinase C-β to increase human neutrophil superoxide generation. *Mol Endocrinol*. 24:813-821.

Shaw AC, Joshi S, Greenwood H, Panda A, Lord JM (2010). Aging of the innate immune system. *Current Opinion Immunol*. 22:507-513.

Expertise

Developing new treatments for rheumatoid arthritis and leukaemia; why getting older has a negative effect on your immune system and makes you more susceptible to infections such as pneumonia

Related media experts

- [Dr Anna Phillips \(/staff/profiles/sportex/phillips-anna.aspx\)](#)

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