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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-clincial 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. In all of her work she aims to translate research findings into interventions, whether lifestyle (exercise) or pharmacological, to improve immunity.

Janet has published over 135 research papers in scientific journals as well as reviews and book chapters in the fields of immunesenescence, chronic inflammatory disease and neuroendocrineimmune biology. Her research is currently funded by grants from MRC, Arthritis Research UK, Research into Ageing, BBSRC, ESRC, the European Commission and the BUPA Foundation.

She is an enthusiastic communicator of her science and gives frequent talks to groups at both the local and national level, including public lectures at The Royal Society, the Birmingham Science Museum and the British Science Festival. Each year she organises a one day workshop (AgeWell) for older adults informing them of the work of her Centres and the latest advice for a healthy old age.

Janet Lord is a leading member of the NIHR SRMRC. Find out more about the work of the research centre on the **SRMRC website (http://www.srmrc.nihr.ac.uk/)** .

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

- **BMedSci (/undergraduate/courses/med/biomedical-science.aspx)**
- **MBChB (/undergraduate/courses/med/medicine.aspx)**
- **MRes (/postgraduate/courses/combined/med/health-research.aspx)** /PhD

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.
For a full list of available Doctoral Research opportunities, please visit our Doctoral Research programme listings.

Research

RESEARCH THEMES

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

RESEARCH ACTIVITY

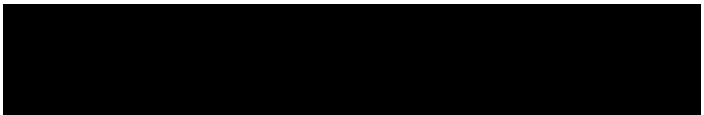
Immune senescence
As humans age they become more susceptible to infectious diseases (especially bacterial infections), inflammatory disease and have poorer responses to vaccinations. Although ageing is a complex process, these data suggest that immune function may be reduced during ageing and will contribute 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. More recently they have been carrying out studies to determine if this reduced neutrophil function has an impact upon immunity in the elderly and more particularly whether stress accelerates this loss of neutrophil function and makes the elderly more susceptible to infection. The group is investigating a variety of stresses that are common in old age, specifically the physical stresses of hip fracture and loss of sleep and emotional stress imposed by depression or bereavement. Her 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). 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. This research is funded by grants from the BBSRC and ESRC (hip fracture studies), Research into Ageing and the European Union (Sleep and Immunity in old age) and the Dunhill Medical Trust (Bereavement and Immunity).

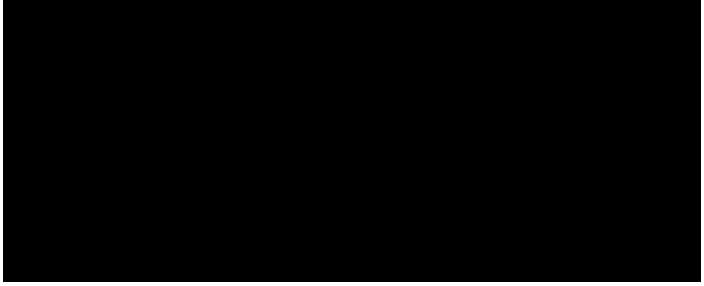
Chronic inflammation
During an immune response inflammatory cells, including T cells and neutrophils, are recruited to sites of infection to help to clear pathogens. Once the site is rendered sterile these same cells must be removed efficiently to avoid non-specific attacks on healthy tissue. This is achieved in part by their death by apoptosis and removal by macrophages. We have 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. Together with Professor Chris Buckley of the department of Rheumatology, the group is trying to define the mechanisms that regulate the survival and activity of neutrophils and T cells within the inflamed joint, in order to identify new therapeutic targets and strategies for Rheumatoid Arthritis. The group has already 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 is funded by a programme grant from the Arthritis Research Campaign.

With funding from the European Union Professor Lord has gone on to use a small molecule library screening approach to identify novel small molecules that are able to regulate neutrophil survival and synovial fibroblast inflammatory function and proliferation (see **http://www.proteinkinase-research.org (http://www.proteinkinase-research.org)**). This has been a productive study which has already identified two novel agents that have reduced inflammation in animal models and work is now ongoing to develop these drugs towards clinical trial.

Leukaemia
The third aspect of Professor Lord's research relates to the search for novel treatments for leukaemia, with a specific focus on targeting the Protein Kinase C family. The PKC family consists of 11 isoenzymes that play different roles in the regulation of cell function and Professor Lord has a particular interest of PKC-delta, which plays a key role in regulating cell survival. She has attempted to identify compounds from natural sources that will modulate the activity of this enzyme, inducing apoptosis in leukaemic cells. Recently she has been working with an Australian biotech company Peplin Ltd (**www.peplin.com (http://www.peplin.com/)**) to take a plant compound, Ingenol 3-angelate (PEP005) through pre-clinical development for acute myeloid leukaemia. Her work has shown that this agent activates PKC-delta and induces cell death (apoptosis) in AML cells at very low doses. Other work in the group has used a small molecule screening approach to identify novel modulators of PKC activity and this has recently yielded a compound which induces apoptosis in chronic lymphocytic leukaemia cells. This agent has been patented jointly with the University of Helsinki and is now undergoing pre-clinical testing. This work has been funded by a 5 year European commission FP6 integrated project and by Peplin Ltd.

Janet discusses her work into Stem Cells and Ageing in this podcast:





Other activities

- Member of the MRC Lifelong Health and Wellbeing panel
- Member of the BBSRC Ageing working group
- Member of the AGE UK Research Advisory Committee
- Member of the FUTURAGE council of scientists advising on the roadmap for European Ageing research in FP8
- Section editor for the journal Aging Cell
- Co-editor in chief of the journal Longevity and Healthspan

Publications

Khanfer RS, Phillips AC, Carroll D, Lord JM (2010). Altered human neutrophil function in response to acute psychological stress. Psychosom. Med.72:636-40.

Curnow SJ, Fairclough M, Schmutz C, Kissane S, Denniston AKO, Nash K, Buckley CD, Lord JM, Salmon M (2010). Distinct Types of Fibrocyte Can Differentiate from Mononuclear Cells in the Presence and Absence of Serum. PLOS ONE 5 (3):e9730.

Hampson P, Wang K, Milverton L, Ersvaer E, Bruserud O, Lord JM (2010). Kinetics of ERK1/2 activation determine sensitivity of acute myeloid leukaemia cells to the induction of apoptosis by the novel small molecule Ingenol 3-Angelate (PEP005). Apoptosis15:946-955.

Arranz L, Lord JM, De la Fuente M (2010). Preserved ex vivo inflammatory status and cytokine responses in naturally long-lived mice. AGE. 32:451-466.

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Phillips AC, Carroll D, Gale CR, Lord JM, Arlt W, Batty GD (2010). Cortisol, dehydroepiandrosterone sulphate, their ratio and all-cause and cause-specific mortality in the Vietnam Experience Study. Eur. J. Endocrinol. 163:285-292.

Lee W-Y, Hampson P, Coulthard L, Ali F, Salmon M, Lord JM, Scheel-Toellner D (2010). Novel antileukemic compound ingenol-3angelate inhibits T cell apoptosis by activating protein kinase C theta. J Biol Chem285:23889-23898.

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Carroll D, Phillips AC, Lord JM, Arlt W, Batty GD(2011). Cortisol, dehydroepiandrosterone sulphate, their ratio, and hypertension: Evidence of associations in male veterans from the Vietnam Experience Study. *J Human Hypertension* 25:418-424.

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

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Sapey, E. Stockley, J.A. Greenwood, H. Ahmad, A. Bayley, D.L. Insall. R.H., Lord, J.M., Stockley, R.A. (2011) Structural and behavioural changes of peripheral neutrophils in COPD. *Am J Respir Crit Care Med.* 183: 1176 – 1186.

Verschuur C, Dowell A, Syddall H, Ntani G, Simmonds SJ, Baylis D, Gale CR, Walsh B, Cooper C, Lord JM, Sayer AA (2011) Markers of inflammatory status are associated with hearing threshold in older people: findings from the Hertfordshire Ageing Study. *Age and Ageing*. doi: 10.1093/ageing/afr140.

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.

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

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- **Dr Anna Phillips (/staff/profiles/sportex/phillips-anna.aspx)**

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