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Current Fields of Research

Our research involves both basic and translational studies into the pathogenesis and treatment of joint and bone diseases. This is supported by the large clinical cohorts including biorepositories, relevant state-of-the-art technologies, and bioinformatics.

Pathogenesis and treatment of autoimmune rheumatic diseases. The identification of biomarkers that facilitate patient stratification and therapeutic targeting. The role of epigenetics in the development of RA and immunoageing. The role of bone marrow stem cell ageing in musculoskeletal diseases. Development of clinical scoring systems in connective tissue diseases.

Control of inflammatory mediators. Characterisation of regulatory mechanisms of inflammatory signal transduction. Activation and secretion of inflammatory cytokines in health and inflammatory rheumatic conditions.

Bone biology in health and disease. The identification of molecular and cellular regulators of bone turnover. Genetic and metabolic aspects of large joint replacement failure. Pathogenesis of osteoporosis, biomarker discovery and optimal treatment. Development of clinical scoring systems for fracture risk. Understanding of bone fragility in children and optimizing treatments and clinical outcomes.

Selected Publications

1. Cummings, S. R., Ensrud, K., Delmas, P. D., LaCroix, A. Z., Vukicevic, S., Reid, D. M., Goldstein, S., Sriram, U., Lee, A., Thompson, J., Armstrong, R. A., Thompson, D. D., Powles, T., Zanchetta, J., Kendler, D., Neven, P., Eastell, R. (2010). "Lasofexifene in postmenopausal women with osteoporosis." *N Engl J Med* 362(8): 686-696.
2. Kanis, J. A., Johansson, H., Oden, A., McCloskey, E. V. (2010). "A meta-analysis of the efficacy of raloxifene on all clinical and vertebral fractures and its dependency on FRAX." *Bone* 47(4): 729-735
3. Mohanty, S. T., Kottam, L., Gambardella, A., Nicklin, M. J., Coulton, L., Hughes, D., Wilson, A. G., Croucher, P. I., Bellantuono, I. (2010). "Alterations in the self-renewal and differentiation ability of bone marrow mesenchymal stem cells in a mouse model of rheumatoid arthritis." *Arthritis Res Ther* 12(4).
4. Yang, L., Peel, N., Clowes, J. A., McCloskey, E. V., Eastell, R. (2009). "Use of DXA-based structural engineering models of the proximal femur to discriminate hip fracture." *J Bone Miner Res* 24(1): 33-42
5. Cummings, S. R., Ettinger, B., Delmas, P. D., Kenemans, P., Stathopoulos, V., Verweij, P., Mol-Arts, M., Kloosterboer, L., Mosca, L., Christiansen, C., Bilezikian, J., Kerzberg, E. M., Johnson, S., Zanchetta, J., Grobbee, D. E., Seifert, W., Eastell, R. (2008). "The effects of tibolone in older postmenopausal women." *N Engl J Med* 359(7): 697-708.
6. Gordon, A., Kiss-Toth, E., Stockley, I., Eastell, R., Wilkinson, J. M. (2008). "Polymorphisms in the interleukin-1 receptor antagonist and interleukin-6 genes affect risk of osteolysis in patients with total hip arthroplasty." *Arthritis Rheum* 58(10): 3157-3165.
7. Maxwell, J. R., Potter, C., Hyrich, K. L., Barton, A., Worthington, J., Isaacs, J. D., Morgan, A. W., Wilson, A. G. (2008). "Association of the tumour necrosis factor-308 variant with differential response to anti-TNF agents in the treatment of rheumatoid arthritis." *Hum Mol Genet* 17(22): 3532-3538.
8. Nile, C. J., Read, R. C., Akil, M., Duff, G. W., Wilson, A. G. (2008). "Methylation status of a single CpG site in the IL6 promoter is related to IL6 messenger RNA levels and rheumatoid arthritis." *Arthritis Rheum* 58(9): 2686-2693

9. Greetham, D., Ellis, C. D., Mewar, D., Fearon, U., Ultaigh, S. N., Veale, D. J., Guesdon, F., Wilson, A. G. (2007). "Functional characterization of NF-kB inhibitor-like protein 1 (NFkBIL1), a candidate susceptibility gene for rheumatoid arthritis." *Hum Mol Genet* 16(24): 3027-3036
10. Sung, H. Y., Guan, H., Czibula, A., King, A. R., Eder, K., Heath, E., Suvarna, S. K., Dower, S. K., Wilson, A. G., Francis, S. E., Crossman, D. C., Kiss-Toth, E. (2007). "Human tribbles-1 controls proliferation and chemotaxis of smooth muscle cells via MAPK signaling pathways." *J Biol Chem* 282(25): 18379-18387

Current Funding

Arthritis Research UK
Medical Research Council
National Institute for Health Research
Wellcome Trust
Lupus UK
Industrial

Training of Fellows in Research

We have an active programme for training of both clinical and non-clinical fellows including the Academic Clinical Fellowships in Rheumatology and Metabolic Bone Diseases. These positions allow clinicians interested in research to undertake a period in research with the aim of generating preliminary data to support an application for a PhD fellowship. We also have a training programme for non-clinical fellows.

WebPages

<http://www.shef.ac.uk/medicine/infectionandimmunity/units/rheumatology>
<http://www.sth.nhs.uk/services/a-z-of-services?id=228>
<http://mellanbycentre.dept.shef.ac.uk/>