Dr Ann Kelly BSc (Hons) PhD

Senior Scientist

Endocrinology, Diabetes and Metabolism

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About

Ann Kelly is a Senior Scientist in the Centre for Endocrinology, Diabetes and Metabolism (CEDAM). She is responsible for the management of the Diabetes Genetics Research group.

Ann has published original research papers relating to the role of genetic factors in determining the risk of complex diseases, including multiple sclerosis, type 1 diabetes, autoimmune thyroid disease, type 2 diabetes and obesity. She has also authored review articles and book chapters on the genetic basis of type 1 diabetes, with particular emphasis on the role of human leucocyte antigen (HLA) genes. Her work has been funded by Diabetes UK/the British Diabetic Association, the West Midlands Regional Health Authority, the Multiple Sclerosis Society, Novo Nordisk UK Research Foundation, GlaxoSmithKline, Eli Lilly UK and the Biomedical Research Centre, Heart of England NHS Foundation Trust.

Qualifications

- PhD Molecular Genetics 1995
- BSc (Hons) Medical Biochemistry 1990

Biography

Ann Kelly graduated from the University of Surrey in 1990 with a BSc Honours degree in Medical Biochemistry. She joined the Department of Medicine at the University of Birmingham in 1991. Under the supervision of Professor Anthony Barnett and Dr David Francis, she undertook a series of studies investigating genetic susceptibility to multiple sclerosis and type 1 diabetes and was awarded her PhD in 1995. Her postdoctoral work in Professor Barnett's laboratory focused on diabetes (both type 1 and type 2) and, in 2001, she was appointed as a Senior Scientist. She has since been responsible for the management of all the research activities in the laboratory.

Teaching

Teaching programme:

- BMedSci Molecular Medicine course

Postgraduate supervision

Ann is interested in supervising doctoral research students in the following areas;

- The role of genetic factors in the development of type 1 diabetes, type 2 diabetes, associated metabolic phenotypes (obesity, dyslipidaemia, hypertension, insulin resistance) and long-term complications (diabetic nephropathy, cardiovascular disease).

Research

Genetic susceptibility to type 2 diabetes and associated metabolic phenotypes
Ann's current research is focused on identifying the genetic factors that underlie the development of type 2 diabetes, associated metabolic phenotypes (such as hypertension, dyslipidaemia and obesity) and long-term complications in South Asian populations. Individuals of South Asian ancestry have a two-to-four-fold greater risk of developing type 2 diabetes compared with white European subjects, are more likely to be centrally obese and are also more likely to suffer from kidney disease and cardiovascular disease as a result of their diabetes. In collaboration with clinical colleagues from the United Kingdom Asian Diabetes Study (UKADS) group (based in Birmingham and Coventry), University Hospitals Leicester, the Diabetic Association of Pakistan and the Baqai Institute of Diabetology and Endocrinology, Karachi, Pakistan, Ann and her research group have created a large DNA resource for studying the inherited factors underlying the increased risk of these phenotypes. Alongside the studies carried out in Birmingham, the research group is also involved in collaborative investigations with researchers from Exeter and Karachi and are part of the South Asian Type 2 Diabetes Study group, an international consortium of scientists from the UK, India, Pakistan, Singapore, Sri Lanka, Australia, Japan, China and the USA. They are also participating in a global research effort to fine-map diabetes genes in different ethnic groups.

Genetics of autoimmune diabetes
Ann worked on the genetics of autoimmune diabetes for over fifteen years and still has an interest in this area. Recently, her research group and colleagues from Sweden showed that latent autoimmune diabetes in adulthood (LADA) is an uncommon phenotype in South Asians, but is associated with a similar genetic profile to that seen in white Europeans. Her earlier research focused mainly on the role of HLA genes in susceptibility to type 1 diabetes, in particular alleles of the DQA1 and DQB1 loci. She was involved in many of the transracial studies carried out in Professor Barnett's laboratory in the 1990s, identifying alleles and haplotypes associated with the disease in multiple ethnic groups. Her early postdoctoral work involved the creation of an in vitro model of the HLA-DQ6.2 molecule to investigate its role in conferring strong protection against type 1 diabetes. This research identified several amino acid residues that are critical to the stability and function of the molecule. She subsequently went on to investigate the differential expression of DQ alleles associated with susceptibility to, and protection from, diabetes. Her interest in HLA-DQ-encoded protection led to a collaborative study with colleagues at Harvard Medical School, which identified variants in the HLA-DQA2 gene that distinguished between healthy individuals and type 1 diabetes patients carrying the protective DQ6.2 genotype. This suggested that disease susceptibility may map centromeric of the DQB1 locus.

Genetics of multiple sclerosis (MS)
Ann's PhD was based mainly on her studies of genetic susceptibility to multiple sclerosis. She and her colleagues were the first to use a transracial approach to identify the HLA alleles underlying the disease in multiple ethnic groups. She also showed that HLA genotype could be used alongside MRI scanning to improve prediction of progression to multiple sclerosis following presentation with a clinically isolated neurological syndrome of the optic nerve, brainstem or spinal cord. Ann collaborated with colleagues in Denmark and the USA to continue her research on MS after completion of her PhD and participated in the first genetic admixture scan to identify susceptibility loci for the disease in individuals of African heritage (Reich et al, Nature Genetics 2005; 37: 1113-1118).

Other activities

Member of

- Diabetes UK
- The European Association for the Study of Diabetes
- American Diabetes Association

Publications

Rees, S.D., Hydrie, M.Z.I., Shera, A.S., Kumar, S., O'Hare, J.P., Barnett, A.H., Basit, A., Kelly, M.A. (2011) Replication of thirteen GWA-validated risk variants for type 2 diabetes in Pakistani populations. **Diabetologia**; 54: 1368-1374.

Rees, S.D., Islam, M., Hydrie, M.Z.I., Chaudhary, B., Bellary, S., Hashmi, S., O'Hare, J.P., Kumar, S., Sanghera, D.K., Chaturvedi, N., Barnett, A.H., Shera, A.S., Weedon, M.N., Basit, A., Frayling, T.M., Kelly, M.A., Jafar, T.H. (2011) An *FTO* variant is associated with type 2 diabetes in South Asian populations after accounting for body mass index and waist circumference. **Diabetic Medicine**; 28: 673-680.

Patel, A., Rees, S.D.**,** Kelly, M.A., Bain, S.C., Barnett, A.H., Thalitaya, D., Prasher, V.P. (2011) Association of variants within *APOE*, *SORL1*, *RUNX1*, *BACE1* and *ALDH18A1* with dementia in Alzheimer's disease in subjects with Down syndrome. **Neuroscience Letters**; 487: 144-148.

Rees, S.D., Britten, A.C., Bellary, S., O'Hare, J.P., Kumar, S., Barnett, A.H., Kelly, M.A. (2009) The promoter polymorphism -232C/G of the *PCK1* gene is associated with type 2 diabetes in a UK-resident South Asian population. **BMC Medical Genetics**; 10: 83.

Britten, A.C., Mijovic, C.H., Barnett, A.H., Kelly, M.A. (2009) Differential expression of HLA-DQ alleles in peripheral blood mononuclear cells; alleles associated with susceptibility to and protection from autoimmune type 1 diabetes. **International Journal of Immunogenetics**; 36: 47-57.

Rees, S.D., Bellary, S., Britten, A.C., O'Hare, J.P., Kumar, S., Barnett, A.H., Kelly, M.A. (2008) Common variants of the *TCF7L2* gene are associated with increased risk of type 2 diabetes mellitus in a UK-resident South Asian population. **BMC Medical Genetics**; 9: 8.

Husain, Z., Kelly, M.A., Eisenbarth, G.S., Pugliese, A., Awdeh, Z.L., Larsen, C.E., Alper, C.A. The MHC type 1 diabetes susceptibility gene is centromeric to HLA-DQB1 (2008) **Journal of Autoimmunity**; 30: 266-272.

Britten, A.C., Jones, K., Törn, C., Hillman, M., Eckholm, B., Kumar, S., Barnett, A.H., Kelly, M.A. (2007) Latent autoimmune diabetes in adults in a South Asian population of the UK. **Diabetes Care**; 30: 3088-3090.