Anatomical Research at the University of Edinburgh

Anatomy has been taught in Edinburgh since 1505 when the Surgeons and Barber Surgeons were incorporated. Teaching is now based in the historic Old Medical School, where we have been teaching and researching into human anatomy for just over 125 years. The steeply raked Padua-style Anatomy Lecture Theatre acts as a focal point for teaching anatomy. In addition there is large extensive laboratory for wet teaching and a museum hosting a range of historic and educational material which can be entered via the hall seen above. Anatomists are now part of the School of Biomedical Sciences and deliver much of their teaching to undergraduate and postgraduate medical students using innovative approaches and technologies. We are involved in numerous collaborative research projects utilizing human anatomical material that often require participation by students studying for their MSc in Human Anatomy. An example of such a project involves strong links between anatomy and the recently established Clinical Research Imaging Centre at the new Royal Infirmary and the Royal College of Surgeons Edinburgh. Much of this type of work is under the control of Dr Gordon Findlater whilst Dr Fanney Kristmudsdottir plays a significant role in student welfare as Sub Dean for Student Affairs.

The University of Edinburgh has a long and distinguished history of scientific research from the pioneering work of Lister into antiseptics, Romanes and Jamieson in human anatomy, through to Kaufman who arguably discovered stem cells. Today, our research strengths lie primarily in the neurosciences, with dynamic research programmes investigating mechanisms of myelination and synaptic connectivity as well as the application of these studies to debilitating diseases such as Motor Neurone Disease, Multiple Sclerosis and hereditary peripheral neuropathies. Our collaborative work is focused though two key specialist research Centre's within the University: the Euan MacDonald Centre for Motor Neurone Disease Research and the Edinburgh Centre for Multiple Sclerosis Research.

Peter Brophy: Professor of Anatomy

The primary goals of the Brophy group are to understand how the myelin sheath is assembled around nerve fibres, and to reveal the molecular mechanisms by which myelination induces the axonal domains that are essential for rapid nerve impulse conduction. This will provide important insights into the fundamental biology of the vertebrate nervous system and contribute to the development of therapies for human demyelinating diseases.

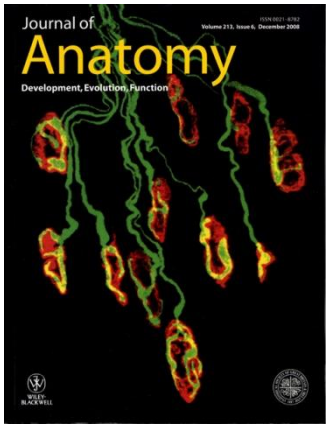
Axon-glial adhesion and signaling - The major site of axon-glia contact is the paranodal axoglial junction. The Brophy group has

found an important glial receptor Neurofascin 155 at this site (J. Cell Biol. 2008; Neuron, 2011). Their Neurofascin knockout mice revealed that Nfasc155 is a glial component of the junctional complex and that Nfasc186 is a major component of the node of Ranvier. These two Neurofascins therefore have essential and unique functions in assembling nodal and paranodal domains of myelinated axons (Current Biology, 2002).

Inherited peripheral demyelinating neuropathy - Brophy's group have also discovered a new dystroglycan receptor complex in the Schwann cell plasma membrane (Neuron, 2003). This Periaxin-DRP2-dystroglycan complex is clustered in a pattern that delineates the "*longitudinal bands*" first described by Santiago Ramon y Cajal in the late 19th century (Nature, 2004, see cover image). The discovery of a mutation in the *Periaxin* gene in a recessive form of Charcot-Marie-Tooth disease (CMT4F) in a Lebanese family demonstrated the importance of these Cajal bands to human peripheral nerve function. In parallel, they generated a mouse model of CMT4F by inactivating the *Prx* gene. The discovery of the PDG complex and the fact that genetically-modified mice lacking Periaxin have disrupted Cajal bands are providing the first insights into the composition and function of these structures (Hum. Mol. Genet. 2001). This work is supported by programme grants from The Wellcome Trust.

Thomas Gillingwater: Professor of Neuroanatomy

Gillingwater's research has focused on investigating mechanisms of neurodegeneration and neuroprotection, with a particular focus on events occurring at the synapse. The majority of work in his laboratory uses mouse models of neurodegenerative disease, with several current projects addressing disease pathogenesis in mouse models of the childhood motor neurone disease, Spinal Muscular Atrophy (SMA). His laboratory routinely combines high-resolution morphological analyses (e.g. transmission electron microscopy and confocal microscopy) with genomic and proteomic technologies. Recent research highlights include studies revealing morphological and genetic factors regulating disease onset and progression in SMA (e.g. Am J Hum Genet, 2004; Hum Mol Genet, 2008; PLoS Genet, 2009; Hum Mol Genet, 2010, 2011), studies examining genetic influences on degeneration and regeneration of the nervous system after injury (e.g. Nature Neurosci, 2001; Brain, 2005; Hum Mol Genet, 2006; Brain, 2006; Mol Cell Proteomics, 2007; J. Anat 2008: see cover image; Genome Biol, 2008; Hum Mol Genet, 2011), and studies examining development of synaptic connectivity *in vivo* and *in vitro* (e.g. J Neurosci, 2006; J Neurosci, 2008; Nature Comm, 2011). Professor Gillingwater also has several collaborative projects with Professor Peter Brophy's group, examining the importance of interactions between glial cells and axons for stability of the nervous system in health and disease. Grant support for research in the Gillingwater lab has been secured from a range of sources, including; the Wellcome Trust, Medical Research Scotland, the BBSRC, BDF Newlife, the SMA Trust, the Anatomical Society, and the Muscular Dystrophy Campaign.



Simon Parson: Senior Lecturer in Anatomy

The Parson group has a long-standing research interest in the peripheral nervous system. From early studies on dorsal route ganglia they began to work on the neuromuscular junction studying receptor and cytoskeletal protein localization at motor nerve terminals (P2X7: J. Neurosci. 2001; Adenosine: Synapse, 2005; Myosin 2: Neuroreport, 2005; Potassium channels: Brain Res. 2004). The Parson group has developed an interest in factors which disturb connectivity at this terminal synapse such as ATP (BMC Neurosci. 2007) and particularly hypoxia. Skeletal muscle has surprisingly low normoxic concentrations of oxygen, but these can still fall dramatically as a result of exercise, vascular disease and traumatic injury. Although muscle itself is highly resistant to hypoxia they have demonstrated rapid disassembly of pre-synaptic motor nerve terminals following hypoxic insult in adult tissue (J. Anat. 2008: See image of motor nerve terminal loss from motor endplates after hypoxic insult from this paper) and a surprising and dramatic resistance to the same insult in neonatal tissue (FASEB, J. 2011). Given the divergence in response to hypoxia, they have gone on to study the nature of oxygen supply to skeletal muscle and therefore the fine structure of the capillary bed, which ramifies through muscle. They have developed new techniques, both morphological and molecular to quantify the extent of the capillary bed. Dr Parson has a close collaboration with Professor Gillingwater on the childhood form of motor neurone disease, Spinal Muscular Atrophy. Their joint work is particularly directed to investigating the role of tissues other than motor neurons in the etiology of this debilitating and fatal disease (Hum. Mol. Gen. 2010a,b, 2011). This work is supported by Newlife Foundation and RS McDonald Charitable Trust.