

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

The Smooth Muscle Group at Dundalk Institute of Technology represents the largest group of researchers studying the physiology and electrophysiology of smooth muscle in Ireland and the UK. We have more than 3 decades experience in this area and have, in the last 10 years, concentrated on examining the ionic mechanisms underlying and modulating contractile activity in tissues as diverse as lymphatic, urogenital, erectile, gastric and cardiovascular smooth muscles from a variety of species including humans.

Our laboratories are equipped with state of the art apparatus and include a facility dedicated to the study of isolated tissues, a patch clamping suite for whole cell and single channel electrophysiology, confocal microscopy facilities for immunohistochemistry, and a cellular imaging laboratory for the study of intracellular regulation of calcium in cells.

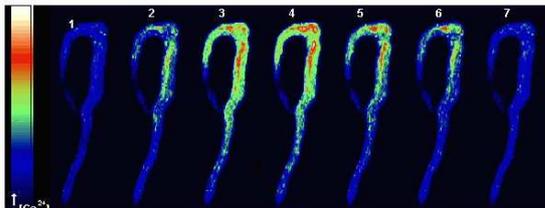


Figure 1. Confocal imaging allows us to observe effects of drugs on Ca²⁺ handling in isolated cells.

Our research team is continually expanding and at present, consists of 5 senior researchers, four post-doctoral researchers and nine graduate researchers. All of our staff are highly

training in each area and provide expertise in a range of techniques applicable including patch clamping,

intracellular recording, calcium imaging, immunohistochemistry & molecular biology.

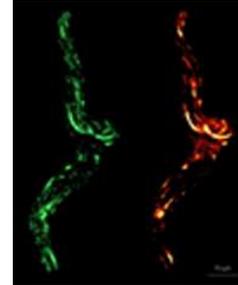


Figure 2. Immunohistochemistry can be used to demonstrate the co-localisation of ryanodine and IP₃ receptors in gastric myocytes.

Our research group has gained prominence at both national and international levels as a result of a number of findings reported by our team. We have demonstrated and characterised the effects of a novel series of compounds that activate a specific type of K⁺ channel in smooth muscle^{1,2}. These compounds may prove to be useful the management and control of disorders as diverse as hypertension and unstable bladder. Our group were the first to successfully isolate and study lymphatic smooth muscle cells^{3,4} and have since uncovered the mechanisms responsible for initiating and modulating lymphatic contractility^{5,6}. Our findings suggest that the electrophysiology of lymphatic smooth muscle resembles that of the heart (see figure 3).



Figure 3. A specialised population of lymphatic cells possess a hyperpolarisation activated current.

Such information is of particular relevance to pharmaceutical companies with an interest in the treatment of oedema.

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

In the last year we have provided evidence to suggest that a specialised group of cells act as pacemakers in the urethra and are responsible for the initiation and modulation of tone within the urethra⁷. These cells (figure 4) differ from the bulk smooth muscle in their gross morphological appearance electrophysiology and immunohistochemistry.



Figure 4. Specialised pacemaking (A) and smooth muscle cells (B) isolated from the urethra.

They fire regular spontaneous action potentials which appear to be initiated by the release of calcium from IP₃-sensitive and Ryanodine sensitive stores⁸. Part of our research team is currently establishing if a similar mechanism is responsible for the modulation of urethral tone in humans. Such research will eventually allow the design of drugs that can preferentially stimulate these pacemaker cells and help to treat stress incontinence.

PhD Projects on Offer

Our group is continually expanding and is always looking for enthusiastic high calibre life science graduates to join us. In particular, we are keen to strengthen our morphology and molecular biology team and would like to hear from graduates with experience in these areas.

With the facilities and expertise on offer

within our research group, we can assure that you have a challenging and rewarding Ph.D project in any of the following areas:

1. Control of Urinary continence
2. Mechanisms underlying lymphatic pacemaking.
3. Cellular mechanisms underlying erectile function.
4. Control of smooth muscle intracellular calcium.
5. Physiology of the microcirculation.
6. Molecular biology of ion channels in smooth muscle.
7. Immunohistochemistry

If you would like to find out more about our group or would like to have a tour of our lab please contact:

Dr Mark Hollywood.
Smooth Muscle Research Centre
Dundalk Institute of Technology
Dublin Road
Co. Louth
Ireland.

Tel: (0044) 0121 288 1798

email: mark.hollywood@dkit.ie

www.smoothmusclegroup.org

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

References:

1. Cotton_KD, Hollywood_MA, Thornbury_KD, McHale_NG. (1996) Effect of purinergic blockers on outward current in isolated smooth muscle cells of the sheep bladder. AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY, 1996, **39**. C969-C973
2. Hollywood_MA, Cotton_KD, McHale_NG, Thornbury_KD. (1998) Enhancement of Ca²⁺-dependent outward current in sheep bladder myocytes by Evans blue dye. PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY, **435**, 631-636.
3. Cotton_KD, Hollywood_MA, McHale_NG, Thornbury_KD. Outward currents in smooth muscle cells isolated from sheep mesenteric lymphatics. (1997) JOURNAL OF PHYSIOLOGY-LONDON **503**, No.1, pp.1-11
4. Hollywood_MA, Cotton_KD, Thornbury_KD, McHale_NG. Tetrodotoxin-sensitive sodium current in sheep lymphatic smooth muscle. (1997) JOURNAL OF PHYSIOLOGY-LONDON. **503**, No.1, pp.13-20.
5. McCloskey_KD, Toland, H. M, Hollywood_MA, , Thornbury_KD, McHale_NG Hyperpolarisation-activated inward current in isolated sheep mesenteric lymphatic smooth muscle. (2000) JOURNAL OF PHYSIOLOGY-LONDON. **521**, No.1, pp.201-211
6. Toland, H.M., McCloskey, K.D., Thornbury, K.D., McHale, N.G. & Hollywood, M.A. (2000). Calcium-activated chloride current in sheep lymphatic smooth muscle. AMERICAN JOURNAL OF PHYSIOLOGY, **279**: C1327-C1335.
7. G. P. Sergeant, M. A. Hollywood, K. D. McCloskey, K. D. Thornbury, and N. G. McHale (2000). Specialised pacemaking cells in the rabbit urethra. JOURNAL OF PHYSIOLOGY, **526**: 359-366.
8. G. P. Sergeant, M. A. Hollywood, N. G. McHale and K. D. Thornbury, (2001). Modulation of pacemaking cells in the rabbit urethra by IP₃. AMERICAN JOURNAL OF PHYSIOLOGY: (in press).