

### Mathis Riehle

History of The Centre for Cell Engineering (CCE) founded in 1997, Adam Curtis, Chris Wilkinson, soon joined Matt Dalby, Catherine Berry, Mathis Riehle. Now joining Manuel's team in Engineering and Andrew Hart and Dominic Meek in Medicine to create and officially introduce the new Centre for the Cellular Microenvironment. New labs in new Research Hub from 2020, shared with Technologies Touching Life groups at UGLA.

### Monica Tsimbouri

Stimulation of osteogenesis in MSCs using a nanovibrational bioreactor (Nanokicking). The group in Glasgow noticed that nanopodia that cells use to cling on the surface interact with nanofeatures around 25nm. Nanoscale topography alone can induce osteogenesis in MSCs. Work with colleagues in France showed that when cells approach a surface they vibrate the membrane. Group in Glasgow designed a new concept to provide cells with nanoscale mechanotransduction, a nanovibrational bioreactor, and found that at 1000Hz and 30nm there was a significant osteogenic effect, without induction chemicals. Latest published results on 3D systems in Tsimbouri et al. Nature Biomed Eng 2017

### Mathis Riehle

Cells, drugs and bioengineered constructs to aid peripheral nerve repair. Work with Suzanne Thompson. Biology of peripheral nerve repair allows natural regeneration (Allodi et al 2012 Progress in Neurobiology) Defects that are under 5mm can be stitched together and the tissue repairs. Defects bigger than 5 - 10 mm need help, as degeneration, scar occurs. Clinical practice is use of autografts, entubulation repair. Both have some advantages and disadvantages. Glasgow team approach is to use a combination of technologies and materials to develop microstructured, porous (swiss roll) membranes that allow diffusion and keep cells in place (Donoghue et al 2014 Mol Pharmacol). In vitro experiments with differentiated adipose derived stem cells (ADSCs), that maintain glial phenotype when cultured on micropatterned polymer. Animal experiments with autologous ADSCs in rat, with 15mm gap model. Coating of the surfaces for enhanced effect. Use of frog foam, that contains proteins displaying adhesion peptides.

### Manuel Salmeron-Sanchez

Engineering systems for efficient regeneration of bone critical sized defects. First (veterinary) patient, dog called Eva. Background of the science for growth factor presentation (published Nature Reviews Materials 2018). ECM-bound presentation vs soluble administration. Enhanced effect of the GF presentation by co-localization: GF binding beside the integrin binding region in Fibronectin. FN globular conformation vs linear (open) conformation on PEA surface and native ECM. Animal model, critical size defect in mouse radius. In vitro and in vivo experiments published in Science Advances 2016. Plasma coating and 3D printing ongoing development in FABW project. Ongoing work with hydrogels, synthetic based, with ECM proteins, GFs, to control the cell microenvironment in 3D systems.

### Andrew Fagan (Licor)

Near-infra red fluorescent imaging, in vivo imaging

### Ben Arnold (ThermoFisher)

Very big company! A bit of everything.

## Sue Barnett

"Proliferate" commercial scaffold based on cross-linked poly-e-lysine for CNS repair (spinal cord)  
Complicated injury process, scar formed with astrocytes in CNS compared to PNS. Current repair strategies, to fill cysts/damage tissue, look to prevent secondary damage and maintain glial and neuronal survival, get rid of inhibitory signals for repair. Glasgow team approach is to use a biodegradable scaffold to fill damage area and in the future support cell transplantation. Scaffolds must allow cell attachment and migration, optimal porosity to allow flow (40-200um). Good survival and proliferation of cells in vitro. In vivo, contusion model in rats of spinal cord injury (SCI), good integration of implant. However, GFAP + Astrocyte border persists after 7 weeks.

## Neal Millar

Inflammatory mechanisms in tendinopathy. Limited treatment options. Stress and damage in the tendon causes inflammation where degeneration and regeneration compete. Mechanisms in Millar et al Nat Rev Rheum 2017. Trial in equine tendinitis of a mir29a replacement, reduces collagen 3 levels, maintains collagen 1 levels, improves healing. Planned phase 1 trial in humans. Spin out company. Other study with protein interleukin (IL)-17A, a cytokine that regulates and stimulates inflammatory process. Target, using antibody to bind and block it. Phase 2 trial ongoing with Novartis.

## Cosimo de Bari

The regenerative biology of the synovial joint. The synovium is a reservoir of "joint stem cells" work to study these cells (joint interzone cells) in their native environment. Development of a functional assay to identify these cells, a mice model of injury of the knee joint surface (Eltawi et al Osteoarth Cartil 2009). Label-retaining (double-nucleoside, Gdf5) cells in synovium proliferate after joint surface injury (Kurth et al Arthritis Rheum 2011), retain MSC phenotype markers, and can be traced in mice model (Roelofs et al Nature Comm 2017)  
Yes-association protein (YAP) activity is linked to MSCs proliferation, synovial lining hyperplasia after injury. Gdf5 lineage cells in mice model, have good chondral regeneration, low osteogenic. Adult human synovial MSCs retain joint morphogenetic properties in adult life.

## Sanjay Gupta

Tumor surgery - collaborative research, clinical work. Surgery + radiotherapy has high risk of infection. Looking for alternatives. Branding, marketing of clinical studies, to enroll/recruit patients. Register in clinicaltrials.gov, have a website, easy name. Several barriers for clinical research: knowledge of stats, ethics, chasing partners, extra work and funding.

## Robert Wallace

Microstructure and time-dependent mechanical response of bone. Bone is arranged in trabeculae in particular at the end of bones where load is received and transferred. Bone is viscoelastic (stiffer to quick loads) and viscoplastic (will stretch more with loads over time), mechanical properties are time-dependent. Study of the microstructure of trabecular bone in the femoral head. uCT scans of the head, region specific analysis, dissected samples tested in compression. Microstructure changes, is rearranged, with increased strain. Finite element simulations developed for time dependent properties, screw loosening. Effect of lower density bone on creep, load sharing. Application to better designs.

## Robert Silverwood

3D osteoprogenitor culture model. Several techniques tested. (i) Magnetic levitation, culture on magnetic nanoparticles. Not very good for long term viability. (ii) Hanging drop system, better viability, more expensive. (iii) Ultra-low attachment technique (bottom of well-plate), good viability.

### Jon Clarke

Management of knee disorders

Research work done with computer aided surgery, enhanced recovery, work now with synthetic meniscus scaffold (Actifit), characterization of mechanical properties.

### Helen wheadon

Bone marrow morphogenic signals in sustaining chronic myeloid leukaemia. CML is a stem cell disease. Current TKI treatment suppresses the disease but not cure. Also patients can acquire TKI resistance over time. More targets needed, understanding of morphogenic pathways in the bone marrow niche.

### Ewan Ross

Nanotopographies influence in MSCs metabolism. Square (SQ) topographies increase glycolysis

### Stuart Reid

Contribution to the Nanokicking bioreactor, how the nanometer vibrations it produces have been measured and calibrated using the expertise of working on the measurement of gravitational waves. Use of interferometer principles. Use of finite element simulations to design a vibrational platform with homogeneous distribution of the vibration. Development of the several evolutions of the bioreactor device, culture-ware and packaging considerations. Applications to osteogenesis and other tissues, also control of bacterial biofilms.

### oana Dobre

3D hybrid laminin based hydrogels for bone regeneration.

Bone regeneration and bone grafts overview, over 2.2M grafting procedures annually worldwide. Interest in GFs and cytokines as therapeutic candidates. Research inspired to develop systems that deliver GFs with mimicking strategies in the native ECM: (A) affinity of biomaterial matrix and GFs, (B) engineer signaling microenvironment, (C) engineer GFs to interact with biomaterial matrices, (D) and engineer GFs to bind biomaterials or endogenous matrices. Work with ECM protein laminin, involved in cell adhesion and migration and present in most adult organs. It has several isoforms, with different participation in regenerative processes. Work with laminin 111 and laminin 511 in bone regeneration. Hydrogels made with Acrylate-PEG systems. Photo crosslinked or



Michael type addition, with different PEG acrylate concentrations. Mechanical properties, degradation with collagenase. Release of VEGF in mouse laminin 111 hydrogels: slower release than BMP-2 suggests higher affinity of VEGF to mouse laminin. With human laminin 111 hydrogels: slow release of BMP-2, higher affinity of BMP-2 to human laminin 111 than to mouse laminin 111.