King's-China Scholarship Council (K-CSC) Programme

Supervisor Catalogue Supplement

Faculty of Dentistry, Oral and Craniofacial Sciences
November 2020-21

This document is an updated list of supervisors in the Faculty of Dentistry, Oral and Craniofacial Sciences at King's College London interested in taking China Scholarship Council funded students in the 2020-2021 academic year.

Please go to
https://www.kcl.ac.uk/study/assets/PDF/graduate-school/k-csc-2021-supervisor-catalogue.pdf
for the full list and to

https://www1.kcl.ac.uk/graduate/funding/database/index.php?action=view&id=308

for information on instructions on how to apply.

You are strongly encouraged to email potential supervisors to express your interest as early as possible.

Centre for Craniofacial & Regenerative Biology

Supervisor: Professor Agamemnon E Grigoriadis

Email: agi.grigoriadis@kcl.ac.uk

Online profile: https://kclpure.kcl.ac.uk/portal/agi.grigoriadis.html

Project title: Pluripotent stem cell approaches for bone and cartilage tissue engineering

The ability to regenerate bone and cartilage tissues efficiently for treatment of bone trauma, and age-related disorders such as osteoporosis and osteoarthritis is currently an unmet need in skeletal health. Stem cell-based therapeutic approaches provide a promising route to tissue regeneration, but this has proved to be very difficult in part due to the lack of suitable defined progenitor cell populations that can form stable and functional tissue. We have developed model systems for efficient generation of specific osteoblast and chondrocyte progenitor populations through directed differentiation of pluripotent stem cells (ESCs, iPSCs), that yield mature bone and cartilage tissues both in vitro as well as in in vivo xenograft models. The current PhD projects will be aimed at combining these defined cell populations with specific biomaterials that have specific chemical and physical properties that will drive stem cell differentiation and support formation of either bone or cartilage tissues. These are essential studies for translating these findings to therapeutic settings. This project is aided through collaboration with tissue engineering and biomaterials laboratories within the KCL Dental Institute as well as with international stem cell laboratories.

Project title: Regulation of bone tumour formation and metastasis

Osteosarcomas are primary bone tumours that affect children and young adults. Survival has reached a plateau of ~70% but has not improved in the last 20 years. Importantly, survival of patients with lung metastases drops significantly to 15-20%. There is therefore an urgent need for development of targeted therapeutics for both primary tumour formation as well as tumour cell dissemination and metastatic disease. We have developed an animal model for osteosarcoma and have identified different cell signaling and kinase pathways that drive lung metastasis. The current PhD projects are aimed at investigating the effects of small molecule inhibitors that are targeting kinase pathways *in vivo* for osteosarcoma metastasis, as well as identifying novel immunoregulatory pathways that mediate tumour growth and resistance to chemotherapy. This project is aided by collaboration with oncology groups within the KCL Cancer Centre as well as bone tumour pathologists and orthopaedic surgeons nationally and internationally.

Supervisor: Ciro Chiappini

Email: Ciro.chiappini@kcl.ac.uk

Online profile: http://chiappinilab.com

Research Areas/projects:

- Engineering nanomaterials for intracellular delivery in regenerative medicine

Co-Supervisor: Prof. Al-Jamal

This exciting project aims to investigate the mechanisms activated by the interaction of cells with nanomaterials and leverage them to control the intracellular fate of the cargo. The work follows up on our research on the biointerface of nanoneedles for drug delivery outlined in Chiappini et al. Nat Mater 2015, Gopal et al. Adv Mater 2019. Geometry and surface chemistry of nanomaterials are crucial in determining their interaction with cells and the fate of the cargo, but there is still a pressing need to understand how nanomaterials can be designed to leverage specific cellular processes that direct cargo to the cell cytoplasm and nucleus. This project will address these challenges blending nanotechnology, biophotonics with cell/molecular biology.

- Engineering Extracellular Vesicle Payloads using Nanoneedles

Co-Supervisor: Prof. Dazzi

Extracellular vesicles (EVs) play an important yet poorly understood role for intracellular communication. They are attracting growing interest as effective nanodelivery platforms that reduce toxicity and improve targeting. Yet, the limited ability to engineer their payload composition hampers the potential of EVs as cell-instructive elements for cell biology, tissue engineering and oncotherapy. Here we engineer the payloads of EVs by leveraging the upregulation of endocytosis induced by nanoneedles. Combining our expertise in drug delivery with that in the isolation, formulation and characterisation of EV we aim to develop a step-changing strategy to formulate nanoparticle-enriched EVs for delivery of biologicals.

- Recapitulating the tooth mesenchymal stem cell niche in vitro.

Co-Supervisor Prof. Sharpe

The ultimate goal of this project to develop a bioengineered niche that reproduces the in vivo cell transitions from mesenchymal stem cells to transient amplifying cells to odontoblast and fibroblasts, in a maintained, controllable way. To achieve this we will generate a microfluidic device hosting the engineered niche consisting of adjacent microenvironments. We envisage that four microenvironments will recapitulate the niche. In the first environment we will present the conditions to maintain stem cell self-renewal. In the second environment, adjacent the first, we will stimulate formation and manteinance of TACs. The third and fourth environments, both adjacent to the second, will induce differentiation towards odontoblasts and fibroblasts respectively.

Supervisor: Professor Philippa Francis-West

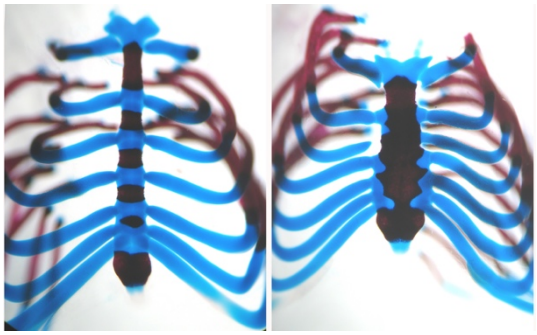
E-mail: philippa.francis-west@kcl.ac.uk

Online profile: https://kclpure.kcl.ac.uk/portal/philippa.francis-west.html

Project description:

Making and Shaping bones by the Fat-PCP-Hippo pathway

The aim of the research team is to understand the role of the Fat4-Dchs1 signalling pathway during mammalian development. This is an essential pathway for human development as mutations in Fat4 and Dchs1 result in Van Maldergem's syndrome characterized by a number of developmental defects including altered craniofacial development. Fat4 and Dchs1 act together to coordinate cell polarity and growth via the Hippo pathway. Fat4 and Dchs1 mouse mutants have alterations in cell organization and proliferation which alter the development, size and shape of bones. The bones in mutants can be shorter and wider (e.g. sternum) or smaller (e.g. cranial bones). This project will investigate how Fat4 and Dchs1 control skeletal development by analysing cell shapes and organization within developing bones and the identification of transcriptional targets of Fat4-Dchs1 signalling.



These are alcian blue and alizarin red stained sternum and ribs from a wildtype (left picture) and a Dchs1 mutant (right picture) mouse showing the altered sternum development in a Dchs1 mutant. In the mutant the sternum is shorter and wider. This is due to a failure of the sternal cells to change their cell orientation and then move towards each other during development. For further information see Mao Y, Kuta A, Crespo-Enriquez I, Whiting D, Martin T, Mulvaney J, Irvine KD, **Francis-West P.** Dchs1-Fat4 regulation of polarized cell behaviours during skeletal morphogenesis. Nat Commun. 2016 May 5;7:11469.

Supervisor: Prof Karen Liu

Co-supervisor: Prof Marie Therese Hosey, Head of Paediatric Dentistry

E-mail: karen.liu@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/karen-liu

Project description:

Novel Genetic Causes of Craniofacial Birth Defects

Craniofacial malformations are among the most common birth defects and are a major cause of infant mortality. Children with these conditions frequently require surgical repair, which can be extensive, and many are left with chronic medical and social issues. However, despite the impact of these anomalies on infant and child health, we have only a rudimentary understanding of the genetic causes. Even for the most common disorders such as cleft lip/palate and craniosynostosis, the majority of cases have no known genetic association. One of the key difficulties is to definitively identify which genes are relevant and why these mutations are pathogenic. To address this problem, we will combine clinical genetics and developmental biology approaches in order to link findings in the clinic to studies in the research laboratory.

Supervisor: Professor Andrea Streit

E-mail: andrea.streit@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/andrea-streit

Project Title: Human ear organoids: modelling ear development and disease

The sense of hearing is critical for our communication with the environment and for many aspects of normal life. Hearing impairment ranks among the world's 10 most common disabilities and is the most common birth defect affecting sensory systems. In children, hearing loss causes difficulties in the acquisition of language and in the development of cognitive functions, while in the elderly it leads to isolation and depression and has been highlighted as a dementia risk factor. 70% of childhood deafness is due to genetic mutations, but many of the causative mutations and genes have not been identified. To make progress we need to understand better normal development of the human ear and the genetic network that controls it.

This project combines stem cell biology with modern molecular methods to study human ear development and to understand how genetic mutations affect this process. The student will use human induced pluripotent stem cells to optimise the formation of ear organoids in vitro, use transcriptional profiling to investigate cell diversity and compare this with existing data collected from cells isolated from developing embryos. Human ear organoids also offer the opportunity to test how mutations identified in patients lead to ear malformations and ultimately result in hearing loss. These studies will help diagnosis of hearing loss, genetic counselling and in the long-term will lead to the development of new therapeutic approaches. The project benefits from collaborations in stem cell biology, genome engineering and imaging in within King's and abroad.

Project Title: Making ears from sensory stem cells

A key question in biology is: how do cells with the same genomic information become different from each other. This is not only important to understand normal development, but also to determine what goes wrong in disease, how we can use this information to promote tissues regeneration or to reprogram cells for stem cell-based therapies. This project explores how stem cells in the embryo generate the ear, the sense organ responsible for sound and balance, using modern developmental and molecular approaches.

We have recently defined many factors that describe the transition of stem cells to ear identity, as well as the epigenetic mechanisms that regulate them. Human homologs of these factors map to known deafness loci where the causative gene has not been identified. This project aims to:

i) explore the role of these candidate genes in ear formation using in vivo gain- and loss-of-function approaches and establish how their mutation causes deafness in humans;
ii) build a 'wiring diagram' for ear formation that serves as a model to predict new deafness genes and the outcome of genetic mutations.

The student will use state-of-the-art molecular methods including RNA- and ATAC-sequencing, combined with in vivo approaches to study gene function. This will include standard analysis of gene expression and conventional and confocal imaging to study cell behaviour. Ultimately, this approach will generate a road map for how cells become committed as ear cells, and this will help to design ways to reprogram cells and to improve genetic diagnosis and treatments for hearing loss.

Supervisor: Dr Isabelle Miletich

E-mail Isabelle.miletich@kcl.ac.uk

Online profile: https://kclpure.kcl.ac.uk/portal/isabelle.miletich.html

Joint second supervisors: Prof Karen Liu and Dr Bethan Thomas

Project description:

Molecular mechanisms underlying parotid and accessory parotid gland formation

Most of the saliva is produced by three pairs of major salivary glands (SGs) including the parotid glands (PGs) located at the back of the mouth in front of the ears and the submandibular and sublingual glands that are both located in the floor of the mouth. 20% of the human population also exhibit accessory parotid glands (APGs), which represent ectopic PG salivary tissue that is located separate from and anterior to the main PG. The etiology of APG formation is currently unknown and understanding the mechanism behind APG formation would be valuable for salivary gland tissue regeneration. The research project will take advantage of our transgenic mouse line that develops bilateral APGs with 100% penetrance. The project will focus on three aspects:

- **Aim 1.** Most of the research on SG development has focused on the submandibular gland and little is known on PG development. The first aim of the project will **characterise the normal development of parotid glands** with a focus on epithelial stem/progenitor cells and innervation, which have been shown to play a key role in submandibular gland development.

- **Aim 2. The timing and cellular and molecular changes preceding APG formation** will be studied in our APG mouse model.

- **Aim 3.** *In vitro* cultures of embryonic PGs will be set up, which will allow to manipulate the levels of known signaling pathways with small pharmacological molecules to **model APG formation *in vitro***.

The project will use transgenic mice and a range of techniques including quantitative PCR, immunohistofluorescence, *in situ* hybridization, *in vitro* organ culture and imaging with conventional and confocal microscopes.

Centre for Host Microbiome Interactions

Supervisor: Prof. Luigi Nibali

Email: Luigi.nibali@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/luigi-nibali

Project Title

Oral Infectogenomics: how host genetic variants can affect the composition of the oral microbiome

Recent research shows that host genetic variants can affect the colonization by specific microbes. The terms 'Infectogenomics' and 'Genetic dysbiosis' were introduced to define the effect of host genetic variants in influencing microbial colonization in a given ecological niche, which could lead to an imbalance between the integrity of barrier organs and their colonizing microorganisms. Animal models suggest an increase in gut dysbiosis in the presence of predisposing pro-inflammatory genotypes.

The plan of this PhD is to improve our understanding of oral infectogenomics by exploring how host genetic variants affect subgingival, salivary and gut microbiota. This will be performed by detailed analysis of the association of host genetic variants and metagenomic analyses of samples of salivary and subgingival plaque. An analysis will be carried out to assess interactions between oral and gut microbiomes. In the era of personalised medicine, knowledge of how host genetic variants influence which microbes colonise our bodies will ultimately improve our ability to treat diseases due to aberrant host response to the microbial challenge, such as periodontitis.

Supervisors:

Dr. James Garnett

Prof. Mike Curtis

Email: james.garnett@kcl.ac.uk

https://www.kcl.ac.uk/research/garnett-lab-fodocs

https://www.kcl.ac.uk/people/mike-curtis

Project title:

Structural and cellular studies of the Porphyromonas gingivalis type-IX secretion system and vesicle biogenesis

Project description:

Bacteria produce outer-membrane vesicles (OMVs) via blebbing of the outer-membrane, although how they form is unclear. OMVs are decorated with proteins and polysaccharides and are important for progression of bacterial disease. *Porphyromonas gingivalis* is a Gram-negative pathogenic bacterium of the oral cavity and causes chronic periodontitis. It uses a type-IX secretion system (T9SS) to export virulence factors, which are then covalently attached to the cell surface via a specific type of liposaccharide (A-LPS) and also sorted into OMVs. Anchorage of A-LPS to the outer-membrane is mediated through the lipid A component of the molecule. We have determined that the T9SS regulates the phosphorylation status of lipid A via a lipid A phosphatase (LpxE), and this is essential for correct OMV formation.

The overall aim of this PhD project is to provide atomic insight into how the T9SS and A-LPS are able to regulate and influence the formation of OMVs in *P. gingivalis*. This project will involve anaerobic culturing of *P. gingivalis*, creating mutant strains and OMV isolation. Proteins will be expressed in *Escherichia coli* and purified for structural biology studies (Cryo-EM, NMR, crystallography). Gaining molecular insight here will allow us to understand new biological processes but may also present novel drug targets for developing new antibacterial compounds. CSC Project - JAG_MAC

Supervisors:

Guy Carpenter (Kings College London)

Thomas Reddyhoff (Imperial College).

Email: Guy.carpenter@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/guy-carpenter

Project Title: How tribology affects taste

The taste of foods is modified by saliva which covers the taste buds located on the tongue. During oral processing of foods (ie eating and drinking) there are considerable shear forces generated by the tongue moving against the palate. These shear forces can be modelled experimentally by measuring tribology of real samples of saliva and food. In this project we will assess the factors affecting the tribology of saliva and the delivery of tastants to electronic taste buds. In the first instance we will examine the transport of salt but in further experiments the physical properties of artificial sweeteners will be assessed in order to replace sucrose.

This project will use a range of techniques as well as tribology. Biochemical assessment of saliva and proteins, formulation of taste solutions and ultimately some in human experiments maybe used to validate any findings found experimentally. A good understand of mathematics would be an advantage but no previous skills are necessary.

Supervisor: Dr Mandeep Ghuman

E-mail: mandeep.ghuman@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/mandeep-ghuman

Project title: Secretome-based approach to enhance periodontal regeneration

Periodontitis (gum disease) is a chronic inflammatory condition which results in the progressive destruction of the supporting tissues of the teeth, and ultimately tooth loss if untreated. It has a reported prevalence of approximately 50% of the adult population worldwide, with severe periodontitis being the sixth most common disease of mankind.

Current treatments aiming to regenerate damaged periodontal (gum) tissues can be only be employed in specific circumstances and are unable to correct the most common problem - horizontal alveolar bone loss. Furthermore, they are technique sensitive and produce unpredictable clinical outcomes. Consequently, there has been considerable interest in developing new methods for periodontal regeneration including the use of stem cells.

Direct application of stem cells has been suggested as a promising therapy to promote regeneration of damaged periodontal tissues, but preclinical and clinical studies have so far shown they have limited efficacy when implanted directly. More important than contributing directly to tissue regeneration, stem cells appear to primarily recruit host cells to promote tissue regeneration. A full understanding of these processes may result in the ability to replicate them therapeutically without necessarily having to reimplant stem cells themselves and improve upon current outcomes.

The proposed project will involve *in vitro* cell culture models to investigate common secreted growth factor signalling pathways as well as identification of secreted factors using high throughput transcriptomic and proteomic approaches. Subsequently a preclinical disease model will be used to compare the effectiveness of candidate secreted factors in promoting periodontal regeneration when compared to implantation of cells directly using a scaffold-based delivery system.

It is anticipated that the findings of this project will provide insights into communication between periodontal stem cells and host cells as well as to identify and test effectiveness of candidate molecules.

Centre for Oral, Clinical & Translational Sciences

Supervisor: Professor Owen Addison

Email: owen.addison@kcl.ac.uk

Online profile: https://kclpure.kcl.ac.uk/portal/owen.addison.html

Project title: Improving our understanding of biomaterial associated reactions: the development of novel X-ray fluorescence imaging modalities.

Project description: Metallic biomaterials are used as part of routine healthcare to replace or repair lost or damaged tissues, but current materials are often associated with adverse biological responses. Chronic biological reactions are frequently linked to implant derivatives (metal surfaces, particles, ions, and metal-modified biomolecules), to infection or a combination. This project aims to improve the predictive modelling of materials-biological interactions to reflect chronic long-term phenomena that are relevant to our ageing population. We have recently applied state-of-the-art multimodal imaging approaches to relate material chemistry to *in-vivo* tissue and cellular responses to a range of orthopaedic and dental implant material derivatives. This project aims to: 1) further develop X-ray fluorescence microscopy immunohistochemistry methods to enhance our ability to correlate tissue elemental distributions and the organisation of the tissue response. 2) Develop the use of 2D-X-ray Absorption Spectroscopy mapping to more accurately understand the chemical speciation of implant-derived material in tissue and cellular environments. 3) Develop more 'informed' biological compatibility testing for existing and novel implant alloys (high entropy alloys) based upon findings from objectives 1) and 2).

The student will be immersed into a multidisciplinary environment including support from experts in physics, metallurgy, immunology and clinical sciences. The project will apply state-of-the-art synchrotron X-ray based methods (at national facilities such as the Diamond Light Source, UK and the European Synchrotron Radiation Facility, France) to *ex-vivo* tissue and cellular substrates. These will be complemented by routine and advanced immunological methods including imaging mass cytometry. The student will join a productive group and alongside task-specific training will have considerable opportunity for generic research skills acquisition including presenting at national and international meetings.

Supervisors:

Professor Richard Cook

E-mail: Richard.2.cook@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/richard-cook

Professor Jennifer E Gallagher

Email Jennifer.gallager@kcl.ac.uk

Online profiles: https://www.kcl.ac.uk/people/jenny-gallagher

Project title:

Exploring oral health needs amongst adults receiving palliative care

Project description:

Maintaining oral health is vital for every individual's quality of life. A recent rapid review synthesizing oral health related quality of life are poor and professional support and care for this population is needed. Whilst staff placed value on oral health barriers to providing both routine daily and professional dental care were present. None of the research was longitudinal in nature.

existing evidence on the oral health of adults approaching end-of-life1, has highlighted that oral health and The principle of co-production of solutions with staff and patients is increasingly recognized as an important approach to developing high quality patient-centred responsive healthcare which meets appropriate needs.

The aim of this research is to explore the normative and perceived oral health needs of adults attending palliative care settings (hospices) in south east London over time, and co-design solutions which are acceptable to patients, their families and staff.

Methods will include clinical epidemiological assessment of a cohort of adults and follow-up over their last year of life and questionnaire interviews; interviews and/or focus groups with patients, staff and families to explore how self/assisted care and professional care might best be provided in and through the centre, with a view to testing viable solutions.

Supervisor: Dr. Mark Ide

E-mail: mark.ide@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/mark-ide

Re-exploring links between periodontitis and pregnancy outcome

Controversy still exists in terms of the potential impact of maternal periodontitis on pregnancy outcome and positive effects of oral health interventions on this.

Whilst associations do appear to exist in some population studies, these have not been consistently found, and there is similar inconsistency around the outcomes from professional interventions.

Newer research data suggests that modified interventions may be of benefit, and that this may be used in conjunction with easily accessible biomarkers to provide a novel targeted approach to therapy. However for this to be realised it is first necessary to validate these approaches using a combination of clinical and translational approaches.

This proposed project would offer the opportunity to commence these studies in one of several multidisciplinary approaches as part of the pathway for a new approach to preventing adverse pregnancy outcomes.

Periodontitis, oral health, inflammation and cognitive impairment

There are increasing data supporting relationships between poor oral health and potential bacteraemia as a driver of systemic inflammation and the potential for impact on cognitive health.

However there are still challenges in terms of identification of at risk individuals and the potential for oral health interventions to impact on this proposed inflammatory axis.

This multidisciplinary and translational project will employ a range of methodologies to validate novel screening tools and biomarkers for periodontitis and cognitive decline, to relate these to microbiome and to inflammatory status and hence to determine if interventions are likely to be successful in impacting cognitive decline.

Supervisor: Dr. Lorenzo Veschini

E-mail: lorenzo.1.veschini@kcl.ac.uk

Online pofile: https://www.kcl.ac.uk/people/lorenzo-veschini

Project:

Creating mature vascular networks in vitro

Cell behaviour is affected by their micro- environments consisting of extra-cellular matrix, other cells and growth/morphogenetic factors dynamically regulated in space and time. It is essential to recreate these micro-environments in vitro to understand cell behaviour and signalling in response to stimuli.

Investigating how variation in perfusive flow affects the maturation and functions of vascular networks is key to understand the molecular mechanisms underpinning cellular flow sensing and development of vascular diseases such as arteriosclerosis.

It is currently possible to recreate vascular tubules in vitro by self-assembly of endothelial cells and pericytes under appropriate stimuli but continuous perfusion of these networks is not possible with current technologies.

Cellular micro-environments and perfusion can be recreated in vitro on biocompatible microchips employing microfluidic technology (lab-on-a-chip, LOC). We have developed perfusable LOCs for the study of angiogenesis and vascular maturation. Our current LOC doesn't allow continuous perfusion as this would require specific adaptations of the platform such as the design and manufacture of a LOC-to-word connections and connection to perfusion pumps.

In this project we will address these challenges.

1) We will design a novel LOC-to-world connection platform to perfuse engineered vascular networks
2) We will investigate the responses of primary (Aortic, coronary, saphenous vein) and human induced pluripotent stem cells (hiPSC)-derived endothelial cells to variation in perfusive flow at the functional and molecular level.

We will employ state-of-the-art technologies such as DLP-3D printing, directed hiPSC differentiation and high-troughput/high-content image analysis.

The project will be run within the academic centre of reconstructive science (ACRS) with access to state-of-the-art facilities for 3D Printing and training opportunities in a variety of subjects e.g. stem cells cultures, micro-fabrication and automated image analysis (including scripting languages and bioinformatics).

Supervisor: Professor Mahvash Tavassoli

Email: mahvash.tavassoli@kcl.ac.uk
Online profile: https://www.kcl.ac.uk/people/mahvash-tavassoli

Project title: The contribution of tumour derived exosomes to therapy resistance in head and neck cancer

Project description:

Head and neck cancer is the 6th most common cancer with over half a million new cases diagnosed each year worldwide. More than 90% of cases are head and neck squamous cell carcinomas (HNSCC). HNSCC remain hard to treat and survival rates have not improved for over 30 years. Epidermal growth factor receptor (EGFR) is often aberrantly expressed in HNSCC and this has been associated with aggressive disease and poor prognosis. In recent years, various EGFR-targeting drugs have been developed and approved for clinical use; but these drugs show only limited effect and many patients become resistant. The reasons for acquired resistance to EGFR inhibitors are currently unknown. One possible explanation for the lack of success of these treatment strategies is the focus of current research on the cell autonomous functions of the receptor, namely its mutations and overexpression. However, it is known that vesicle mediated cell-cell communications occur in the tumour microenvironment and EGFR itself can be released in a special form of vesicles called exosomes. While the intracellular activities of EGFR have been extensively studied, little is known about the contribution of exosomal EGFR to tumorigenesis and therapy resistance. We have recently shown a role for tumour derived EGFR containing exosomes in HNSCC (https://www.ncbi.nlm.nih.gov/pubmed/30142511).

The student will analyse a panel of HNSCC cell lines for their inherent sensitivity towards EGFR targeting drugs using cell viability assays. He/she will generate HNSCC cell lines with acquired drug resistance by treating sensitive cell lines with increasing doses of EGFR-targeting drugs.
Exosomes of sensitive and resistant cell lines will be isolated, and their EGFR content will be compared using immunoblotting. Sensitive cell lines will be treated with exosomes isolated from resistant cell lines and the effect on cell viability in the presence of EGFR-targeting drugs will be analysed. This project will deepen the understanding of the contribution of exosomal EGFR to the success of EGFR-targeting drugs.

Impact on student: This project allows the student to work in an innovative and exciting field of translational research in an international and collaborative research environment. It will additionally introduce him/her to the most common molecular biology and cell culture techniques as well as more specific techniques such as Nanosight, CyTOF, Flow cytometry. Comet assay and others..
These techniques are transferrable skills useful in many areas of biological research and required for many industrial and academic jobs. The day-to-day supervision will be undertaken by a senior lab member while the overall supervision will be by the PI. The research fellow will experience all steps involved in the scientific research process starting with the formulation of the research question, the design of the experiment as well as the hands-on performance of the experiment followed by the analysis of the results. This will greatly improve his/her critical thinking and analytical abilities. The student will attend lab- and divisional meetings as well as national and important international conferences, which will provide further insight into related fields of research.

Supervisor: Dr. Trevor Coward

E-mail: trevor.coward@kcl.ac.uk

Online profile: https://www.kcl.ac.uk/people/trevor-coward

Project:

Manufacturing implants for maxillofacial reconstruction by PEEK 3D printing

Surgery following cancer or injury in the maxillofacial region can result in large bone and soft tissue defects. Current gold standard for treatment of these defects is autologous bone transplantation which is limited in its application by donor-site availability and morbidity.

Creating artificial scaffolds for bone tissue engineering have raised much attention from the scientific community in the past years but very few materials have reached clinical application.

Main defects of artificial scaffolds are the scarce ability to integrate with host tissue and thus to provide long-term benefits to the patients. Poly-ether-ether-ketone (PEEK) is a n FDA/CE approved material for the fabrication of maxillofacial implants but not differently from other materials possess very scarce osseointegration capacity. Furthermore, PEEK implants are currently manufactured by milling (subtractive manufacturing) which involves significative material waste and thus increased implant's costs.

3D printing (additive manufacturing) has recently become a viable alternative to PEEK milling to manufacture implants of desired shape.

In this project we will develop a novel manufacture workflow of maxillofacial implants based on 3D printing. Furthermore, we will functionalise PEEK with novel synthetic self-assembly peptides which have demonstrated the ability of ameliorating cell adhesion to PEEK in vitro and bioactivity of BCP scaffolds in vivo.

Aims of the project are:

1) To develop a 3D printing pipeline to manufacture PEEK implants of desired shape, porosity and mechanical properties.

2) To functionalise PEEK surface with self-assembly peptides and evaluate biological response of osteoblasts (osteogenesis) and endothelial cells (angiogenesis) which are known cellular functions mediating osseoconduction, osseoinduction and ultimately osseointegration (in vivo).

The project will be run within the academic centre of reconstructive science (ACRS) with access to state-of-the-art facilities for 3D Printing and training opportunities in a variety of subjects e.g. cell-biology and automated image analysis (including scripting languages and bioinformatics).