

## Feline cholangiocyte organoids – An interspecies approach to investigating feline and human cholangiopathies

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**Co-supervisor:** Prof Penny Watson (Veterinary Medicine)

**Research area:** Organoids, regenerative medicine, veterinary science

### Project outline:

The bile ducts are a network of tubes draining bile from the liver to the intestine. Bile duct disorders (cholangiopathies) are a major cause of liver failure in humans and animals. Treatments are minimal because of our limited understanding into the disease pathogenesis, and the lack of laboratory models for drug development. The only therapy for end-stage cholangiopathy in humans is liver transplantation, which is not available for most animals (e.g. cats).

To address these challenges, our lab pioneered the culture of bile duct cells (cholangiocytes) as organoids, and used these organoids for disease modelling, drug screening or cellular therapy to regenerate damaged ducts, instead of transplantation.

We propose to apply this organoid technology to feline cholangiopathies, in collaboration with Dr Watson. Cats provide excellent candidates for two reasons. First, liver transplantation is not an option, lowering the barrier for regenerative medicine therapies. Second, the disease phenotype differs from human. Feline cholangiopathies do not cause scarring, which leads to liver failure in human. Dissecting the differences in cholangiocyte organoids between the two species could identify pathways promoting scarring in human.

### Aims

1. Generation of cholangiocyte organoids and cholangiopathy models from feline tissue
2. Comparison of human and feline cholangiopathy models to identify therapeutic targets in humans and cats
3. Feline organoid injection in cat livers ex-vivo as a new therapy for feline biliary tract disease

This project will shed light in the pathogenesis of cholangiopathies in cats and humans, identify potential therapeutic targets and pioneer regenerative therapies for veterinary medicine

**BBSRC DTP main strategic theme:** Bioscience for an integrated understanding of health

**BBSRC DTP secondary strategic theme:** Understanding the rules of life, Transformative technologies