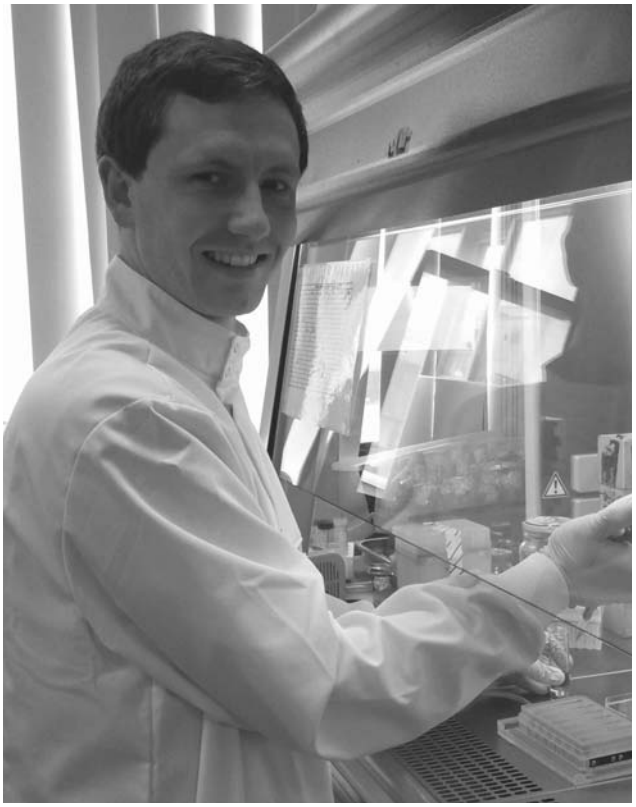
# News from the FAL

**The FRAME Alternatives Laboratory currently has 10 postgraduate students, who are researching human-based replacements for animals in drug discovery and toxicity testing. Here, two of our newest recruits describe the projects they are working on.**

My name is Richard Maclennan, and I'm a first year PhD student in the FRAME Alternatives Laboratory (FAL) at the University of Nottingham. I graduated in June 2011, with an undergraduate BSc (Hons) degree in Molecular Medicine from the University of Sussex, and started a postgraduate PhD with FRAME in October 2011. My work at the FAL involves the development of a dynamic cell culture system that allows the cells to retain the characteristics of the human liver for long periods of time, and which can be used in toxicity testing for the identification of substances that might cause liver cancer. The tests currently used to screen for liver tumour development involve dosing rodents with a test compound, or drug, over a period of up to two years, and then examining the liver for signs of tumour growth. These tests often cause pain and stress to the animal. Furthermore, results from animal-based tests might not translate well to the clinic or the environmental settings in which humans would be exposed to these drugs and compounds. In fact, the same substance has been shown to perform in completely different ways in rodents and humans. In some cases, the animals exposed to a particular drug or compound did not develop any hepatic abnormalities, whereas human exposure caused adverse reactions in the liver and tumours. The reverse situation can also occur. The disparity between the data from animal models and human exposure is a result of fundamental differences in cell signalling and response pathways between rodents and humans. Therefore, we need to develop human-based systems to tackle problems that are particular to the human body.

My name is Louis Brailsford, and I graduated with a BSc (Hons) in Biochemistry from the University of Nottingham in July 2011. I joined the FAL the following September, to start a PhD studying the development of osteoarthritic pain. Osteoarthritis (OA) is a painful degenerative joint disease that is caused by the breakdown of the firm flexible cartilage tissue on the surfaces of the joint, leading to inflammation



*Richard Maclennan*

*Louis Brailsford*

and excessive bone breakdown. Excess bone reabsorption of the joint surface has been implicated in the development of OA, and is thought to be a contributing factor in osteoarthritic pain. Therefore, as bone breakdown is mediated by a group of cells known as osteoclasts, attenuating osteoclast activity could represent a therapeutic opportunity to treat, not only one of the causes of OA, but also blockade the source of pain generation from the joint. My research focuses on elucidating the cellular signalling mechanisms in osteoclast development and activity at the molecular level, by isolating osteoclast precursors from the blood of human volunteers and culturing these cells *in vitro*. Dissecting the underlying complex signalling networks will allow us to assess the effects of candidate drugs on osteoclast development and activity. The use of human cells as an alternative to animal testing will reduce animal suffering, and, because the cells are of human origin, will offer the opportunity to develop a much more relevant drug discovery system for osteoarthritic pain.