The construction of heart modelling leads path to new therapies

January 10 2008

Heart disease is still a major killer, especially in the western world, but new therapies based on stem cells and other techniques could now be imminent. Progress is being held back however by the difficulty testing new therapies on human heart tissue, with animal models being only of limited value owing to differences in structure and activity. The only solution in the absence of real human models is to create computerised "in-silico" models that simulate the real heart and enable possible drugs and therapies to be tested without risk to people. Although this is still some way off becoming a reality, substantial progress has been made, and the next steps were plotted at a major workshop held recently by the European Science Foundation (ESF).

The workshop highlighted how recent progress in imaging technologies was helping heart modellers overcome the big dilemma they have faced up till now – actually proving that the models really are an accurate representation of the real human heart. This has been the big "catch 22" of heart modelling, that in order to create a realistic model, you need accurate and extensive data from real hearts for calibration. "Validation of the models is very important, and was raised at the workshop," said Blanca Rodriguez, scientific coordinator of the ESF workshop, and senior cardiac researcher at Oxford University, Europe's leading centre for cardiac modelling. "One of the problems has been that it is much easier to get experimental data from animals than humans."

Such animal data can help calibrate some aspects of the models, but only data from human hearts can fine tune them to the point at which they

can actually make useful predictions and test therapies. Fortunately such data is now becoming available as a result of dramatic progress in imaging techniques that can observe cardiac activity externally without need for invasive probes. “We are now getting data at very high resolutions, and that allows us to model things in more detail, with greatly improved anatomy and structure,” said Rodriguez. This in turn requires access to greater computational power and more sophisticated software, both of which are available at Oxford.

The models in turn are allowing researchers to study disease and understand what can go wrong, which is the first step towards developing cures. One of the most important diseases being modelled is myocardial ischaemia, which is the loss of blood supply to part of the heart muscle, leading ultimately to failure and potentially death if untreated.

Typically victims of heart failure never fully recover their former health and vigour, because part of the heart muscle has been permanently lost. However stem cell therapy holds the promise of being able to regenerate heart muscle destroyed by disease, but this will require careful testing to eliminate possibly dangerous side effects, such as cancer and disruption of normal heart rhythms, leading to arrhythmia, or irregular heart beats. Here again the heart models could play a vital role. “They could be used to model stem cells’ behaviour, and see how they are incorporated into the heart,” said Rodriguez.

The ESF workshop also had another dimension – to kick start a Europe-wide effort to catch up with the US in this vital field. Oxford was once the world leader, for remarkably the first cardiac model was developed almost half a century ago in 1961 by Dennis Noble, who although now officially retired is still assisting Rodriguez and colleagues today. Noble’s original model was of just of a single heart cell. But since the late 1990s, the models have been extended to the whole organ, incorporating multiple cell types.

The workshop identified three key issues that had to be addressed, according to Rodriguez. The first one was to improve the links within Europe's scattered heart modelling community. The second two recommendations, less specific to Europe, were to create a standard and robust software infrastructure for sharing heart models and associated data, and to define exactly how to calibrate the models more effectively from experimental data.

The next step is to act on these recommendations, but Rodriguez is now confident that Europe is well placed to regain its early momentum in this vital field of medical research.

Source: European Science Foundation