

FOCUS ON RESEARCH

GENETIC BASIS OF THE RESPONSE TO EXERCISE AND INACTIVITY – DESIGN OF NOVEL GENETIC MARKERS OF DISEASE RISK

Researchers

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Aim

This project aimed to develop ways of identifying novel genes that are either switched on or off during exercise in human bone. The intention is to use this information to design drugs that can mimic the positive aspects of exercise and to identify “exercise genes” that are not functioning properly in certain individuals.

Project Outline/Methodology

Exercise is very important in the maintenance of the amount of bone that we have but unfortunately as we age there appears to be a decrease in our ability to build bone with exercise. Therefore there is a need to understand what molecules are produced by cells in bone during exercise so that we can determine what goes wrong during ageing and diseases such as Osteoporosis. We have studied the effect of exercise on live human bone in a novel bioreactor system that can apply exercise stimuli equivalent to a person walking or jumping. We can use this system to measure:

- i) how much bone is formed in response to exercise.
- ii) to find out if exercise can keep the sensor cells alive in bone so that they can function properly
- iii) to very accurately describe the genes that are switched on when we undertake load bearing exercise.

Key Results

When bone was not exercised in the bioreactor the numbers of live sensor cells (osteocytes) were shown to decrease. Applying mechanical stimuli to bone maintained these cells alive and furthermore the jumping form of exercise was shown to be more beneficial than the walking form of exercise. Markers of bone formation were increased on exercise and using a technique called microarray we were able to look at the response of 38, 5000 genes within cells of bone. When Exercised samples were compared to Control samples 260 genes were found to have significantly higher expression and 121 genes significantly lower expression in response to jumping exercise. While many of these genes are already known to be responsive to exercise in animal studies, here for the first time, we show they respond in the same way in human bone. However of particular

importance is the identification of an entirely new set of genes that are responsive to exercise in human bone.

Conclusions

Our study has proved very successful in the identification of new exercise genes and this information has not only increased our understanding of the exercise response in bone but has also pointed to some novel areas in which we might design new drugs to combat bone loss in the elderly.

What does this study add to the field?

The development of techniques capable of applying exercise stimuli to live human bone represents an entirely unique opportunity to study in detail the response of bone cells to exercise in their natural environment. Novel, exercise responsive genes have been identified. The use of human bone in our system not only allows for the first time the study of exercised human bone but also removes the requirement for the study of these responses in animals.

Implications for Practice or Policy

We currently have a poor understanding of genes that predispose an individual to a positive bone related response to exercise. The use of our gene expression data for the identification of genetic markers of disease risk will be beneficial.

Where to next?

We are currently seeking funding so that we can maximise the information gathered during this study. Not only will this data facilitate exciting new areas of future research in cellular mechanotransduction but will potentially foster the design of pharmacological agents to stimulate the important cell saving and bone anabolic effects of exercise in individuals unable to do so. This will be of particular importance with respect to an ageing population.

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