A model of how to introduce school students to biochemical research

MBP^2

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How many secondary schools do you know, where Sixth Form students can be part of an original research programme involving a human gene transformed into bacteria and yeast?

I only know of one – The Simon Langton Grammar School for Boys in Canterbury. For the past 16 months, students have been engaged in the Myelin Basic Protein Project – or MBP^2 for short. They are learning and using a range of biochemical and molecular biology techniques. Students in the Sixth Form are attempting to understand more about the structure of Myelin Basic Protein (MBP), the second most abundant protein in the myelin sheath.

MBP is a very unusual protein; it has no fixed tertiary structure and a vast range of post-translational modifications and has consequently defied attempts to crystallize it. Our working hypothesis is as follows, when MBP is phosphorylated, its fragile structure is distorted. This starts to denature the protein and plays a part in triggering an autoimmune response which ultimately causes de-myelination of axons and the formation of plaques or scleroses. De-myelination leads to the neurological disease Multiple Sclerosis.

Two years ago I had little knowledge of MS, however following my wife's diagnosis with MS, I decided to study the disease further. I considered MBP an interesting protein and then started to wonder if I could attract funding for a research project I could involve our students in. One possibility seemed to be the Wellcome Trust. As part of their Public Engagement programme they offer People Awards, which can extend to £30,000 for up to three years. I applied for an Award at the end of April 2008 and by mid July I heard that we had been successful.

Students at work (Wellcome Images)

Dr Dave Colthurst in the Laboratory (Wellcome Images)

The project focuses on human MBP. We had to apply for a site licence from the Health and Safety Executive to allow us to work with the human gene in *E. coli* and *S. cerevisiae*. The plan is to transform the human gene into *E. coli*, then bulk up the plasmid and manipulate the gene to allow the transfer to a yeast plasmid and add a hexa-His tag. Once this is achieved, we will transform the plasmid into *S. cerevisiae* and look for expression of the human protein.

We are working in yeast because it is a safe organism, suited to a school laboratory. It also shares a high degree of similarity with humans in terms of its biochemistry. We will be looking for phosphorylation events by purifying the MBP on a nickel affinity-column and then running SDS-PAGE. Following this, we will run Western blots and probe the membrane with phospho-amino-acid specific primary antibodies. The secondary antibodies will be HRP-conjugated and visualized with 4-chloronaphthol.

The techniques we are using are more commonly taught in the first or second year of an undergraduate degree; however our students have had the opportunity to learn them alongside post-graduate and post-doctoral researchers from the University of Kent. We hold 'collapsed curriculum days' where the students are off timetable for the day and spend the whole time in our Biology Labs learning protocols and how to use the apparatus.

Co-ordinating the students has proved to be a considerable challenge in itself. In the first year, we had sixty students taking part, this year there

are ninety! They are all studying Biology either at AS or A2, however they all get study time on their timetable, where they are able to get into the lab and carry out their part of the research. The students have been divided into six teams, each led by a student Team Leader and a member of the Biology staff. A team focuses on a specific aspect of the project and my task is to direct their efforts and assemble the big picture.

The teams are:-

1. *E. coli* growth and transformation;
2. *S. cerevisiae* growth and transformation;
3. Protein purification;
4. Western blot analysis;
5. DNA preparation and analysis and
6. Bio-informatics

The groups are all a mixture of Year 12 and Year 13 students to ensure continuity.

In the first year, we ran two of the collapsed curriculum days, or MBP^2 days as they became known. In these sessions, students were working in their teams, learning their techniques and beginning to understand the theory behind the experiments. They were encouraged to use their free time to practice the techniques and become more familiar with the apparatus. The first SDS-PAGE gels took 5 hours to be poured, they now take 40 minutes.

We are currently in the second year of the project and we have expanded. The number of students choosing AS Biology has risen from 65 to 90 and we have 45 students studying A2 biology. Of these students, 90 are involved in the project and I now have two days a week to organize and co-ordinate the work. Already, we have held two MBP^2 days. The Year 12 students are familiar with the techniques and we have managed to push forward the research.

We have two strains of *E. coli* transformed with the human gene, one to bulk up the plasmid, the other to look for expression. We have perfected purification of plasmid DNA by mini- and midi-prep spin columns and we are routinely digesting DNA and analyzing it by agarose gel electrophoresis. We have yet to perfect our Western blots. The gels and transfers are working fine, our detection method still needs improvement and we are still trying to get column chromatography to behave. Our bio-informatics team has designed some PCR primers with restriction sites and a hexa-His tag on them, the next step is to get these synthesized and the product cloned into a yeast plasmid.

Loading an SDS gel (Wellcome Images)

There are many aspects of this project that have exceeded my expectations. The most obvious one is the number of students who want to be involved. Another has been the enthusiasm and commitment shown by the Biology staff, they are working flat out either as teachers or as our technician, and they have all worked tremendously hard to make this project happen.

We have been very grateful for the support and encouragement of staff at the Department of Biosciences at the University of Kent. Professor Mick Tuite, in particular, has helped direct the science in the project and encouraged members of the Department to be involved. Our students have attended the labs for a tailor-made workshop and presented their work to the Department.

In addition we have been able to build strong links with the Kent MS Therapy Centre which is adjacent to our school. Many of our students volunteer their support to the Centre in free-periods and help with admin tasks, tidy up or just help to make drinks for the members using the facilities there. The students raised over £2600 for the Centre last year, this included funds from the sponsored walk, a Battle of the Bands, a Quiz evening and a cricket tournament.

The Wellcome Trust award scheme centres on Public Engagement and we have endeavoured to spread the word about the project. As a school we were invited to contribute a stand at the Royal Society Summer Exhibition last year. We had a fantastic time and were able to prove to a wide range of people that you are 'Never too young to be a Research Scientist.' We have created and delivered four 'MBP^2 DNA Workshops' for local Sixth Form students in Canterbury and aim to run six more this academic year, reaching around 200 more students in total.

MBP^2 has proved that it is possible to provide students with an authentic research experience in the school environment. It allows students to carry out practical work they normally only hear about in lessons – this leads to a much better understanding of the science and a much clearer understanding of the careers open to them as they move on into tertiary education.

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