Coco Day - Wolfson Molecular Imaging Centre (WMIC), Manchester

This summer, I spent eight weeks in Manchester at the Wolfson Molecular Imaging Centre (WMIC), a laboratory on the site of The Christie, a hospital famous for its cancer treatment. Correspondingly much of the work done at WMIC is related to cancer research, specifically to PET (Positron Emission Tomography) scans which are used primarily to locate tumours.

The work I have undertaken, however, was a part of a larger research project to do with early diagnosis of Alzheimer's. The current hypothesis is that Alzheimer's is caused by fragmentation of a protein called amyloid precursor protein (APP), widely found in the body, into amyloid fragments. These fragments are 'sticky' and form amyloid plaques in the brain, which cause the onset of Alzheimer's. The purpose of the research at WMIC is to radiolabel a synthesised version of the amyloid peptide with radioactive fluorine, ^{18}F, so that the radiation it emits (once injected into a subject) may be traced using a PET scan. If the amyloid is seen to enter the brain and to begin to cluster, this would be an indication of the onset of Alzheimer's.

The purpose of the project I did was to separate the radiolabelled peptide out from the unlabelled 'cold' peptide; immediately after synthesis, the vast majority of the peptide is still cold, since there is very little ^{18}F available to react. This means the specific activity, i.e. the concentration of radiolabelled peptide, is very low, and if injected into a subject, the signal would be too weak to be useful. The labelled and unlabelled peptides are a very similar size and mass so are very difficult to separate; especially since the separation must be done quickly as the half-life of ^{18}F is only about 2 hours. The easiest way to separate them is using a method called size-exclusion HPLC (High Performance Liquid Chromatography); as the name suggests, this segregates molecules according to their size by passing them along a column; larger molecules pass through quicker.

To that end, I worked to attach a very large molecule (about 8 times the size of the peptide) to the *unlabelled* peptide specifically, to make its mass much larger so the labelled and unlabelled peptide would be separable by size-exclusion HPLC. This involved first oxidising the sugar molecules so they would possess a functional group that would react only with the unlabelled peptide, then carrying out the reaction with the peptide. I experienced various analytical difficulties in 'proving' first that the sugar had been sufficiently oxidised for the peptide reaction to take place, and several different sugar molecules were trialled, but in the end it worked. There were then several weeks of optimising the reaction, varying different parameters such as temperature, pH, the concentration of the various reagents, etc. The work continues now after I have left WMIC, but while I was there we managed to achieve an improvement in specific activity of 50%, which was very good.

Working at WMIC provided many other exciting opportunities for me as well – for example, the building had an on-site cyclotron to generate radioactive isotopes, and coincidentally I arrived in the week it was closed for cleaning and testing so I got to see inside it! Although Health and Safety requirements wouldn't allow me to handle radioactivity myself, it was very interesting to be in the lab and watch the other scientists doing it – the 'hot cells' in which the reactions take place are perfectly sealed and lined with 10 centimetres' thickness of lead. A computer programme is used to tell the system what to do, which is very different to how I am used to carrying out chemistry – i.e. with my hands!

Overall it was a great opportunity for me to see what it might be like if I choose to take up a career in research, and also to have some experience writing a scientific paper in collaboration with others, which will hopefully be put up for publication soon.