**Carboxylic acid drugs and chemicals – investigating their potential to trigger idiosyncratic liver injury and an auto-immune liver disease**

BTS Vacation Scholarship 2019

By *Justina Grigalytė*

This 8 week placement provided me a great flavour of what it is like to work in toxicology field, which was the main motive why I chose to spent my summer in Professor Wright‘s lab. On the first day I arrived to the lab having the mindset that all of my experiments would go as planned, however, I realised shortly after that it is not the case in research. I routinely performed immunohistochemical staining (IHC), Native PAGE, Western Blotting and learnt the basis of Cell Culturing.

During the first four weeks I was investigating the effects of long-term oral and intraperitoneal (i.p) dosing of M8OI (a chemical recently found to be contaminating the soil around a nearby landfill) in mouse liver tissue by immunohistochemical (IHC) staining. M8OI belongs to a class of chemicals called ionic liquids. Former work in my supervisor’s laboratory demonstrated that ionic liquids, following metabolism to a carboxylic acid, may be capable of triggering primary biliary cholangitis (PBC) [Probert et al. An ionic liquid induces hepatic progenitor apoptosis and has the capacity to replace lipoic acid in a PBC autoantigen. *Journal of Hepatology* **69**, 1123–1135 (2018). <https://doi.org/10.1016/j.jhep.2018.06.027>].

To examine both studies I used primary anti-active caspase 3 antibodies. α-Naphthylisothiocyanate (ANIT)-treated mouse liver tissue and mouse liver tissue without a primary antibody acted as a positive control and a negative control, respectively. The results indicated that there was no liver apoptosis in the mouse i.p M8OI study.

It was hypothesised that drugs and chemicals containing a carboxylic acid would be incorporated into the α-ketoacid dehydrogenase complex (PDC-E2) *in vitro* due to mimicking lipoic acid structure, thus, having a potential to trigger primary biliary cholangitis (PBC). To test the hypothesis, Native PAGE and Western Blotting were carried out. The Western blot indicated that only PFOS and PFNA were incorporated into the PDC-E2 complex, however, to test the validity of the results, further experiments using different concentrations of chemicals needs to be performed.

I was very fortunate to have spent two months in Professor Wright‘s lab because I realised how interesting toxicology research is. I have learnt the importance of good lab practice, as I was handling carcinogens such as DAB, acrylamide, as well as corrosive solutions, such as concentrated hydrochloric acid and sodium hydroxide. I have become competent in optimising experiment conditions. Due to the tissue slides being overstained with DAB, I was trying to find the optimal time to keep the DAB solution on. IHC troubleshooting helped me to engage with the technique and improve my problem-solving skills. With the help from Professor Wright and his PhD student Tarek Abdelghany I learnt to design experiments and work independently most of the time, thus I feel that my confidence in a lab increased considerably. As I will be conducting my third-year project in Toulouse, France, this experience has given me a massive boost to study even harder for my third year and provided me with strong technical skills needed to work independently.

Thanks to British Toxicology Society I had an opportunity to undertake this summer project. I am also very grateful to Professor Matthew Wright and Tarek Abdelghany for support and feedback given throughout the placement.