BDIAP Intercalated Bursary report

- **Full Name**: Mirna Elghobashy
- **Year Bursary awarded**: 2021
- **Medical school**: University of Birmingham
- **Degree**: BMedSc Clinical Sciences

- **General background of the course:**
  My course was split into two semesters; the first semester was predominantly taught modules while the second was fully research focussed. My chosen modules were statistics, bioinformatics, endocrinology and women's health. For each module, I completed two weeks of teaching, written coursework and examinations. In the first semester, there was also 6-weeks of dedicated research time.

- **My research project:**
  My laboratory project was entitled "**Investigating the effect of magnesium in the context of glaucoma and trabecular meshwork dysfunction**".
  Glaucoma is the leading cause of irreversible blindness, affecting over 70 million people worldwide. The main risk factor for the development of the most common form, primary open angle glaucoma (POAG), is raised intraocular pressure (IOP). Pressure builds within the eye due to reduced drainage of aqueous humour, usually resulting from scarring of the trabecular meshwork (TM). Dysfunction in the TM is due to inherent mitochondrial dysfunction, increase in reactive oxygen species (ROS) production and TGFβ-2 induction, leading to a sustained inflammatory response.
  Magnesium is a common intracellular cation, involved as co-factor in over 300 reactions. It is tightly regulated within cells and its particularly important in energy-depended reactions and the mitochondria. Magnesium deficiency has been observed in POAG and is linked to inflammatory and fibrotic responses, as well as increased oxidative stress (OS). Magnesium supplementation been shown to reduce cellular ROS, alleviate mitochondrial dysregulation and has further antifibrotic and anti-inflammatory properties within ocular tissues, and other soft tissues prone to fibrosis, suggesting that magnesium can improve visual fields in patients with POAG.

  The overall aim of my project was to assess the impact of magnesium therapies on reducing the trabecular meshwork dysfunction seen in POAG. During my intercalation, the effects of magnesium chloride on TM cell ROS production, fibrosis and viability were assessed using immunocytochemistry and cell viability assays. I conducted all experiments, conducted fluorescent microscopy and analysed the resulting data.
  Initially, the cells were exposed to varying concentrations of TGFβ-2 in order to simulate a glaucoma model. Next TM cells were exposed to varying concentrations of magnesium chloride hexahydrate, ranging from below physiological levels to above physiological levels. A live-cell stain was used to assess mitochondrial reactive oxygen species production while α-SMA and fibronectin immunocytochemistry were used to assess fibrosis. LDH and MTT assays were used to assess cytotoxicity and proliferation respectively.
  The results showed that magnesium has a dose-dependent effect on ROS production, fibronectin and α-SMA deposition, but had no impact on proliferation and cytotoxicity. The concentrations closest to physiological concentrations of magnesium led to the biggest reduction in ROS production and fibrosis. This is likely due to tight intracellular levels of magnesium required for optimum cellular functioning and metabolism. As this is the first study of its kind assessing the impact of magnesium on TM cells, it is difficult to draw concrete conclusions, however, it may be that magnesium supplementation could be used to alleviate fibrosis in POAG in the future.

- **My intercalation experience:**
  I had an incredibly fulfilling intercalation year and graduated with a first-class degree. I am extremely grateful to BDIAP for their support during my intercalation year. Not only did I have the opportunity to gain research experience, I was also fortunate enough to be investigating a largely untapped topic in literature. With the help of my supervisor and her team, we also published a paper regarding the role of magnesium in glaucoma pathogenesis and its potential as a therapeutic and credited BDIAP for their support – I have attached a PDF of the paper with the outgoing email.
  This intercalated year was invaluable to me and I am sure it will be of great benefit during my foundation applications this year.