**Four year studentship funded by FoodBioSystems DTP**

**Project Title**: Investigation of the capacity of a diet rich in lutein and zeaxanthin to increase macular pigment density, thereby potentially reducing the risk of age-related macular degeneration by dietary means.

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**Research Group**: FOODBIOSYSTEMS BBSRC DTP
**Project ID:** FBS2021-96

**Application details**:
For more details on the application process, please go to the FoodBioSystems website. To submit an application, please go to our studentship application portal (https://foodbiosystemsdtp.grantplatform.com).
Closing date for applications is 12 August 2021, 9.00am BST
Interview date is 19 August 2021. Please note this is a very short timescale due to the inflexible start date of the project.

**PLEASE NOTE:** Due to very strict funding requirements, this studentship is available only to individuals who are eligible for home student fees status and who are available start their studentship **on or before** 30 September 2021. If you are unable to meet these conditions please do not apply because we will not be able to process your application.

**Project Details:**
**Research question**
Can consuming a healthy plant food, rich in protective macular pigments, be a lifestyle strategy that has the potential to reduce the risk of age-related macular degeneration (AMD)?

**Hypothesis**
Consumption of a diet rich in the xanthophylls, lutein and zeaxanthin, can increase protective macular pigment as effectively as a lutein/zeaxanthin supplement, thus potentially reducing the risk or progression of AMD by dietary means.

**Background and Justification**
AMD is the leading cause of blindness in developed countries[1]. In early AMD, waste material, known as drusen, builds up under the retina, the light-detecting layer in the eye[1]. Increasing size and number of drusen is associated with development of the late forms of AMD: geographic atrophy (GA) where there is gradual death

of light-detecting cells and neovascular AMD (nAMD) where fragile blood vessels grow below and into the retina, causing bleeding. Both types lead to permanent vision loss and can occur together. Currently, the only effective treatment for nAMD is eye injections that help reduce vision loss. There are no known treatments to prevent the development of GA[1].

The macula is a specialised part of the retina, mediating central vision, providing the sharpest visual acuity and facilitating the best colour discrimination[2]. Macular pigment, as measured by macular pigment optical density (MPOD), is concentrated in the inner and central layers and is believed to protect against AMD[2]. It is mainly composed of the xanthophylls, lutein, zeaxanthin and meso-zeaxanthin (synthesised *in situ* from lutein)[2]. The concentration of these xanthophylls in the macula is 1000-fold greater than in the blood, demonstrating high selectivity. This suggests a pivotal role for the xanthophylls which are believed to play a major role in protecting the retina and retinal pigment epithelium from light-initiated oxidative damage by scavenging reactive oxygen species and filtering blue light[2]. The xanthophylls are transported on HDL and polymorphisms in HDL-related loci have been associated with AMD and plasma lutein/zeaxanthin[3].

Data from epidemiological studies suggests that dietary lutein and zeaxanthin intake are inversely associated with the risk of AMD. The AREDS2 randomised trial, carried out in the US, supplemented patients with early AMD with an antioxidant supplement that included lutein (10 mg) and zeaxanthin (2 mg). In a secondary analysis of that study, supplementation with lutein and zeaxanthin was protective against progression to late AMD in individuals with low lutein/zeaxanthin intake[4]. A meta-analysis of 19 studies showed that supplementation with lutein and/or zeaxanthin and/or meso-zeaxanthin improved MPOD both in AMD patients and healthy subjects, with a dose-response relationship[2]. However, not all studies have shown an effect of lutein/zeaxanthin supplementation on MPOD[5,6]. The proposed research will address that uncertainty.

**What the student will do:**

- Search the literature to review the evidence for an effect of lutein/zeaxanthin and associated factors on AMD risk and progression.
- In collaboration with Professor Paul Fraser, Head of the Plant Molecular Sciences group at Royal Holloway (and Syngenta), select non-GMO *Capsicum* varieties that are rich in lutein and zeaxanthin.
- Analyse the two selected *Capsicum* varieties for lutein, zeaxanthin, beta-carotene and vitamin C.
- Work with Odysea to produce jars of the selected flame-roasted dark-orange *Capsicum* in brine.
- Recruit volunteers with a family history (therefore at significantly increased risk) of AMD who will agree to consume approximately ½ a *Capsicum* per day (either the selected fresh or bottled variety), or a lutein/zeaxanthin supplement (as a comparator).
- Measure their dietary intake (including lutein/zeaxanthin) by food-frequency questionnaire (FFQ).
- Organise the measurement of macular pigment optical density (MPOD) at baseline and after 13 and 26 weeks of consumption of the *Capsicum*-rich diet *vs.* the supplement in the volunteers.
- Measure lutein, zeaxanthin and cholesterol in blood serum at baseline, 3 and 6 months.

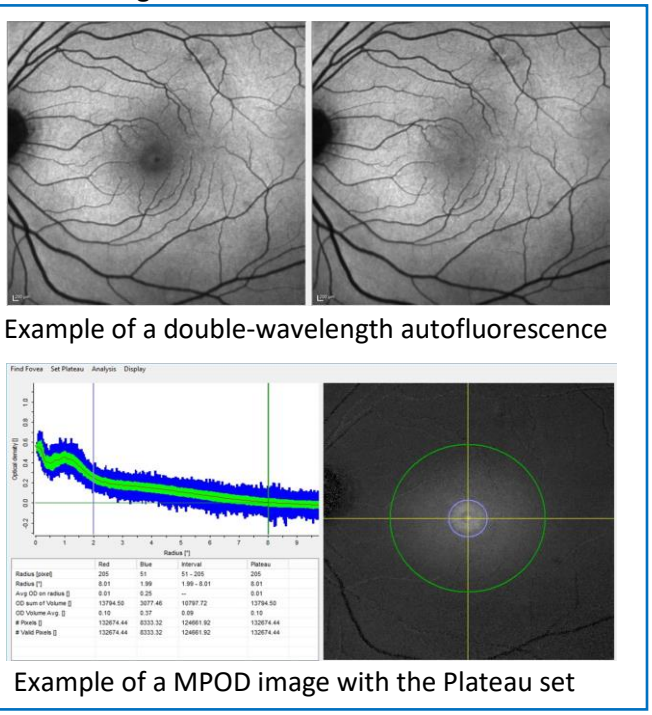
**Funding Notes:** This project is part of the FoodBioSystems BBSRC Doctoral Training Partnership (DTP), it will be funded subject to a competition to identify the strongest applicants. Due to restrictions on the funding, this studentship is only open to students with established UK residency who can prove eligibility for home student status. The funding will include a tax free stipend and support for tuition fees at the standard UK rate (in 2021/2022 this is a minimum of £15,609 per year and £4500 per year respectively). There will also be a contribution towards research costs.

The FoodBioSystems DTP is a collaboration between the University of Reading, Cranfield University, Queen's University Belfast, Aberystwyth University, Surrey University and Brunel University London. Our vision is to develop the next generation of highly skilled UK Agri-Food bioscientists with expertise spanning the entire food value chain. We have over 60 Associate and Affiliate partners. To find out more about us and the training programme we offer all our postgraduate researchers please visit https://research.reading.ac.uk/foodbiosystems/.

- Syngenta has agreed to provide the *Capsicum* varieties specially bred to be high in xanthophylls.
- The student will spend some time in Prof Paul Fraser's laboratory at Royal Holloway to gain an understanding of how the *Capsicums* are bred in collaboration with Syngenta and to analyse the two selected varieties for lutein, zeaxanthin, beta-carotene and vitamin C.
- Odysea will arrange harvesting, preparation and bottling of the dark-orange *Capsicum* in brine.

**Training opportunities:** With Prof Paul Fraser's group in Royal Holloway, University of London (RHUL), to learn about strategies used in crop breeding (in collaboration with Syngenta);
With RHUL to carry out the analysis of carotenoids/xanthophylls pigments in *Capsicum* by HPLC-PDA;
With Odysea to learn about *Capsicum* harvesting, preparation and bottling.
The student will:

- learn the principles of breeding *Capsicum* to optimise xanthophyll production
- obtain ethics permission for a human study
- recruit at-risk volunteers to a dietary intervention
- measure:
  - *Capsicum* concentrations of lutein/zeaxanthin, carotene and vitamin C
  - plasma lutein/zeaxanthin
  - fat mass (a confounder of lutein/zeaxanthin bioavailability) by bioelectrical impedance
- organise measurement of MPOD by state-of-the-art method (see figure)
- modify and analyse an existing UK-validated FFQ so it can capture lutein/zeaxanthin intake
- design and analyse other questionnaires that can identify confounders
- learn how to harvest, process and bottle *Capsicum* in brine
- learn the methodology of public health/epidemiology/medical statistics
- understand the pathology, causes and treatment of AMD


Example of a double-wavelength autofluorescence


Example of a MPOD image with the Plateau set

**Student profile:** This project is suitable for a student with a degree in nutrition, chemistry, agriculture, food science or a closely related science who has an interest in diet and health. He/she should have laboratory skills, be able to write well and already have, or expect to obtain, a minimum of an Upper second class honours degree. The student will be based at Queen's University Belfast but will be expected to spend up to 12 months in total at the University of Surrey.

**References:**


1. SanGiovanni & Neuringer. Am J Clin Nutr 2012; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3471204/pdf/ajcn9651223S.pdf
2. Ma et al. Nutrients 2016; https://www.mdpi.com/2072-6643/8/7/426
3. Koo et al. Am J Clin Nutr 2014; https://academic.oup.com/ajcn/article/100/suppl_1/336S/4576438
4. Chew et al. JAMA Opthalmol 2014; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4636082/pdf/nihms720274.pdf
5. Korobelnik et al. JAMA Ophthalmol 2017; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5710391/
6. Lin et al. Opthalmic Epidemiol 2017; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6025894/pdf/nihms975420.pdf