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 AWARDEE REPORT FORM

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| NAME | Lemonia Chatzeli |
| TWITTER HANDLE\* *optional* |  |
| UNIVERSITY | University of Cambridge |
| NAME OF AWARD | Symington Bequest Fund Awards 2024/25 – Round 1 |
| PURPOSE OF AWARD *conference/event attended/organised (full name) with city and dates.* |
| To support a collaborative project with Sonnen’s group on the role of Notch oscillation in salivary gland development.  |
| REPORT: What were your anticipated benefits?*Minimum number of words between 200-400. Please write in coherent paragraphs.* |
| Branching morphogenesis is a dynamic process that involves continues interactions between the epithelium and the surrounding environment that includes the mesenchyme, nerves, blood vessels immune cells and extracellular matrix proteins. Within the epithelium, the tip of a developing duct acts as a source of progenitors that allow tip to undergo sequential rounds of tip duplication and duct differentiation. Therefore the tips in every round of branching need to balance self-renewal (tip duplication) with differentiation (formation of a new duct). We found that the tips balance this process by having a heterogeneous population of progenitors with different self-renewal and differentiation potentials. In particular, tip progenitors high in Notch signalling are more likely to commit towards a ductal luminal fate while tip progenitors low in Notch, are more likely to self-renew and later contribute to all of the 4 main salivary gland lineages (ductal luminal, ductal basal, acinar, myoepithelial). Given that the Notch signalling is highly dynamic and oscillatory during the formation of somites and the pancreas, we hypothesised that such dynamics also exist in salivary glands and could determine the cell fate choice of the progenitors. Tip progenitors with sustained Notch expression could commit towards a ductal fate while progenitors with low Notch expression or random oscillations could self-renew and acquire later a distinct identity. To test this hypothesis we collaborated with Dr Ina Sonnen who is an expert on the role of gene oscillations in organ formation and regeneration. We anticipated that this collaboration would allow us to benefit from her expertise in live imaging of developing tissues, image analysis of oscillatory genes, handling of big imaging data and interpretation of the role of oscillatory pathways in organ formation.  |
| COMMENTS: Describe your experience at the conference / lab visit / course / seminar/ event.*Minimum number of words between 200-400. Please write in coherent paragraphs.* |
| My visit to the Sonne lab at the Hubrecht Institute, Netherlands was for 10 days. During my visit I was very fortunate to be able to use their expertise and their facilities to study the role of Notch oscillation in salivary gland branching morphogenesis. The experiments involved dissecting and culturing E13.5-E14.5 whole developing salivary glands (explants) in an air liquid interface and performing overnight live imaging to capture Hes1 oscillation during the first events of branching. To understand how other signalling pathways could interact with the Notch pathway, some of these salivary gland explants were treated with various signalling modulators. Throughout this period thanks to the very supportive environment I was able to process more than 10 litters and generate a lot of interesting data. In addition to tissue dissection and live imaging, we performed image analysis of Hes1 oscillations on salivary glands. Interestingly, we found that within the bud of the developing duct, where the progenitor cells are located, Hes1 levels are variable with a few cells having very high levels of Hes1 and the majority of them lower levels. This expression is very dynamic with some cells alternating between low and high expression for approximately every 4 hours. I am now in the process of analysing these results in detail to investigate how these variable levels could affect branching and fate decision.  |
| REPORT: In relation to skills, what were the most important things you gained? *(does not apply to equipment grant.* For public engagement/outreach awards what did your audience gain and how did you evaluate success?*Minimum number of words between 200-400. Please write in coherent paragraphs.* |
| My visit to the Sonnen’s lab was very beneficial for my future research and career plans. This fund gave me the invaluable opportunity to understand how to analyse and interpret gene oscillations in tissue morphogenesis. This includes the developing of methodologies that allow tissue explants to grow under the microscope for 12 hours in an air liquid interface with minimal phototoxicity using multiphoton microscopy and light sheet. This creates images of more than 10 Tb per imaging session. To handle such large images the Sonnen group introduced me to a compression software that allows data transfer and long term storage, without compromising the original image quality. In terms of image analysis, I learned how to track individual cells and record Notch oscillations using imagej to analyse the periodicity of the signal. In addition to the technical skills I gained during my visit, I enhanced my collaborative and communication skills. I introduced my research to the Sonnen group which are not familiar with the salivary glands and presented the ideas and the aims that we would like to achieve from this collaborative project. Most importantly, I established new collaborations that will be used for my future applications to start my own independent lab.  |
| REPORT: How do you think you will put this learning experience into practice in the future? For public engagement/outreach awards how with the materials/knowledge generated by this activity be used in the future?*Minimum number of words between 200-400. Please write in coherent paragraphs.* |
| The learning experience gained from my visit will be invaluable for my future research and career progression. The advanced live imaging techniques and the image analysis skills I have developed will enable me to analyse the interactions of other oscillatory pathways such as the Erk signalling in branching morphogenesis using the mouse salivary gland as a model system. In parallel, the data management skills will enable me to manage not only the future data that I will generate from live imaging but also the imaging data generated from my current and my past project on imaging the entire ductal network of human salivary glands. In addition, the data generated from the collaborative project will be used to create new hypothesis for future projects and applications for independent funding. Among the new research questions that can be generated are to investigate the interspecies variations of Notch signalling between mouse and human salivary glands explants or organoids, and the organ specific variations of Notch signalling in branching morphogenesis of different glandular organs. Finally, the networking and collaboration skills I have developed will enable me to introduce my research into new groups and establish new collaborations. This will be vital for my future career plans towards starting my own independent lab.  |
| Data Protection/GDPR: I consent to the data included in this submission being collected, processed and stored by the Anatomical Society. Answer YES or NO in the Box below |
| YES |
| Graphical Images: If you include graphical images you must obtain consent from people appearing in any photos and confirm that you have consent. A consent statement from you must accompany each report if relevant. A short narrative should accompany the image. Answer N/A not applicable, YES or NO in the box below |
| Not applicable |
| Copyright: If you submit images you must either own the copyright to the image or have gained the explicit permission of the copyright holder for the image to be submitted as part of the report for upload to the Society’s website, Newsletter, social media and so forth. A copyright statement must accompany each report if relevant. Answer N/A not applicable, YES or NO in the box below |
| Not applicable |
| SIGNATURE | Lemonia Chatzeli | DATE | 21/12/2024 |

*If submitted electronically, a type-written name is acceptable in place of a hand-written signature*

*File: AS-Award-Report-Form-171023 – International Conference*