Dr Nat Dyment, Ph.D., Assistant Professor at the University of Pennsylvania, has developed novel methods to research tendon and ligament cell development and repair. Seeking to address the gap in knowledge between the mechanical function of tendons and ligaments and the biological drivers that lead to normal mechanics, his aim is to develop new therapeutic strategies for debilitating joint injuries.

Injuries to tendons and ligaments often do not heal on their own and can be difficult to repair surgically. Because of this, people with these injuries often cannot use their joint without significant pain, leading to poorer quality of life. The research conducted by Dr Nat Dyment and his team at the University of Pennsylvania hopes to improve the outcome of joint injury for the many patients affected each year.

WHY RESEARCH TENDON AND LIGAMENT INJURY?

This research seeks to understand the development of normal tendons and ligaments at a cellular level to better understand what happens when abnormalities occur after injury. An improved level of biological understanding, coupled with established understanding of the mechanical function of these tissues, will allow for better recovery strategies to be developed. With almost half of all orthopaedic injuries caused by an injury to tendons or ligaments, the impact of being able to develop better strategies would significantly improve the lives of a large portion of the population.

The importance of tendons and ligaments can be best understood by considering the frequency of their use in day to day tasks. The mechanical function of tendons is to transfer loads from muscle to bone and the role of ligaments is to stabilise joints. Any repaired tissue must be capable of withstanding the same level of use and mechanical force as the original undamaged tissue. Unfortunately, tendons and ligaments do not share regenerative abilities with other tissues, such as muscle and bone, which can repair themselves after injury. Therefore, new treatments are needed to improve the healing response.

Dr Dyment’s research training originated in the field of engineering where he sought to develop therapies to restore normal function to damaged tendons. Extensive work aimed at defining mechanical parameters that lead to normal tendon and ligament function gave rise to the development of a branch of research known as functional tissues engineering (FTE). The development of FTE was pioneered by Dr Dyment’s PhD adviser David Butler, alongside his team and collaborators, at the University of Cincinnati. Their contributions identified success benchmarks for which repair strategies can be compared against.

Since then, research in this field has seen a paradigm shift away from understanding joint mechanics and towards understanding the biological and cellular parameters that lead to normal formation of tendons and ligaments. Dr Dyment shifted his research focus towards understanding how cells within tendon and ligaments function as our limited understanding hampers the ability to develop novel and improved repair strategies.

NEW TECHNIQUES DEVELOPED

The latest research by Dr Dyment’s laboratory seeks to address the existing gap in the knowledge between the mechanical function of native tendons and ligaments and the biological drivers that lead to normal mechanics. His team aims to identify markers that define the cell populations within tendons and ligaments and the biological factors that control their function.

Firstly, to better understand the cellular components of tendons and ligaments, Dr Dyment’s laboratory utilises models where cells fluoresce different colours depending on which genes they express. This allows researchers to define sub-populations of cells by characterising their behaviour.

Above: fluorescent image of a tendon containing cells that are green or red depending on which genes they express. The blue colour is the collagen matrix between the cells. By understanding how these cells are different from each other researchers can design repair strategies to mimic this environment to improve healing.

Enhanced healing: improving prognosis for joints after injury
within tendons are known as tenocytes and they have typically been thought of as a homogenous population. However, research in Dr Dyment’s laboratory has indicated that there is in fact more heterogeneity than previously thought. Similar realisations have been found in other fields such as cancer research where we now know that tumour cells are very different, making targeted therapies difficult. A similar case will likely be found in tendons and ligaments, where researchers will need to develop therapies that precisely target specific types of cells within these tissues. Dr Dyment’s team hopes to identify biological markers that define immature stem cells and tissues over time in these dimensions. What did the diversity of skills amongst your team bring to your research? Our lab works at the interface of biology and engineering to better understand these issues and how to effectively repair them. This takes a diverse team of developmental biologists, bioengineers, and clinician scientists to engineer solutions to these tremendously problems.

Which of the new techniques developed in your lab was the most interesting to work on? The novel fluorescent models used in our lab have opened our eyes to the complexities of tendon and ligament biology. Yet, the histological techniques have allowed us to make sense of these complexities by properly visualising the cells and tissues over time in three dimensions. How will the treatment of joint injury change in light of your research? In the short-term, our lab’s research will define design parameters and standards for future repair strategies. For instance, we will better define how immature stem cells become mature tenocytes. These discoveries will guide future therapies in the clinic, which is the long-term goal of our lab.

What do you hope the “real world” impact of your research will be for patients? I hope that one day, with the help of basic scientists and clinicians, we will be able to get patients back to their normal day to day activities pain free. Whether it’s a basketball player trying to get back on the court or a retired teacher wanting to play outdoors with his grandchildren, we want them to get back to doing these activities as quickly and safely as possible. The laboratory in the Biomedical Engineering Department at the University of Cincinnati. He carried out postdoctoral training in musculoskeletal biology in David Rowe’s laboratory at UConn Health Center where he was awarded a NIH K99/R00 grant. In 2017, Nat joined the Orthopaedic Surgery Department at the University of Pennsylvania. Dr Nat Dyment obtained his BS in Materials Science and Engineering at the University of Illinois at Urbana-Champaign and his PhD in David Butler’s Functional Tissue Engineering Laboratory in the Biomedical Engineering Department at the University of Pennsylvania.