Professors Milan Mrksich and Guillermo Ameer October 27, 2021

Professor Mrksich opened the session by speaking about innovation and technology at Northwestern University. He noted that NU has several thousand faculty receiving almost $900M in funded research. The primary area of research funding is biomedical research. Disruptive innovation is key to research progress. One example of disruptive innovation occurred when VHS tapes gave way to DVDs. The prior technology was completely replaced. Universities are important participants in disruptive innovation. They are able to "dream big" and can tolerate failures as well as achieve amazing success. In the past, industry had a long history of sponsoring university research. Examples include DuPont and 3M. However, these sponsorships have ended over the past decade as corporations have moved away from basic science research. This has allowed universities, hospitals and institutes to grow and play an even larger role in research as the private sector has cut back. Currently there is more than $100B in sponsored research at universities, hospitals and research in the US.

Dr. Silverman's invention of Lyrica in a research lab at Northwestern was also described. In the late 1980s Dr Silverman was working on protein channels in cells with his colleagues. They discovered a molecule that could block one of the channels. This was pregabalin and they quickly realized it had applications for pain control. Northwestern filed for a patient in 2001, and in 2005 it was launched as Lyrica by Pfizer. Northwestern University received approximately $2B in royalties which was used to invest in buildings and recruitment of new scientists. A contemporary example of a faculty start up model is a company called WMR named for three Northwestern scientists. The group worked with venture capital to produce stents for the nasal cavity that release anti-inflammatory materials to assist in breathing. This company is now publically traded.

Northwestern scientists started another company that uses surface chemistry and engineering techniques. Surface chemistry involves a breakthrough technique using a row of chemicals attached to a gold surface. Subsequent novel experiments used a laser that hit the gold plate causing the molecules to accelerate along a tube. Adding enzymes to the chemicals on the gold plate causes chemical reactions that change the mass of the chemicals and also the speed of the peptides along the tube. This is a breakthrough because it allows scientists to assess chemical reactions on a surface. Northwestern investigators published over 50 papers showing these reactions and their applications. This laid the groundwork for discoveries such as novel drugs and shows how this process can be sped up from prior timelines like the development of Lyrica.

One very important potential example of this technology is in cancer. In cancer, cell growth is uncontrolled so the cells don't "turn off." A pharmaceutical company wants to know what protein has stopped functioning and can we come up with a drug that binds to that protein only and blocks its activity. In other words, can we find a drug to turn off this abnormal cell growth? In order to study this, we need to find the molecule and then determine how to turn it off. Pharmaceutical companies have millions of proprietary molecules that can be tested using the approach described above.

To conclude, Dr. Mrksich summed up the new approach to translational scientific research and how it improves the traditional model. The traditional model of academic research in translational science is to have an academic idea, write papers, conduct experiments, and then try to find a company to work with to develop a partnership. This is the model that worked for Lyrica but it took a long time. In the new model (Slide into Start) some of these steps occur at the same time. The academic partner has the basic science idea and tests it out and then partners with commercial entities earlier. Samdi Technology is an example of a company partnership between private equity and Northwestern faculty and former trainees. This is a group of highly skilled scientists who have the basic science expertise to leverage and advance scientific ideas in an expedited and cost effective way.

Focusing on these partnerships has also strengthened the culture between basic and applied science. In addition to the huge success with funding agencies, translational science engages Northwestern students and faculty as they can truly see the impact of their scientific work on human health.

Dr. Ameer next presented about the Center for Advanced Regenerative Engineering (CARE) taking us from the lab to the operating room. Dr. Ameer has an impressive background in scientific research. He combines engineering and medicine in the new field of regenerative engineering. This field creates tools for regeneration or reconstruction of tissues and organs. The center has collaborations within and outside of Northwestern including industry. He next discussed what you need to be successful in this area including:

- A model of dysfunctional tissue remodeling
- Regenerative biomaterials
- Regulatory approval
- User adoption (surgeons and patients)

To bring these compounds to market you have to accomplish many steps including: developing the technology, protecting intellectual property (patents) and forming infrastructure including licensing agreements and/or start-ups. After basic science experiments show initial efficacy, the industry partner has to confirm safety in pre- clinical and clinical models. Finally you have to have FDA clearance/approval based on safety and efficacy data. Once a product or drug is approved, you have to distribute and sell it and it has to be adopted by physicians as well.

An example of this is partnership is Dr. Ameer's research on citric acid. This compound is ubiquitous in beverages, food, skin products and bone. Using citrate based materials scientists can create biomaterials that have certain properties, are scalable, and can be used in device fabrication. Tissue function can be restored using engineered materials. One example is in stents used for vascular obstruction. This platform can also be used to grow bladder cells and help heal chronic non-healing wounds. Diabetic foot ulcers are a large source of limb loss so this is a very scalable area of inquiry. Dr Ameer next covered the application of his work to joint and bone trauma. In the US there are more than 500,000 soft tissue surgeries each year for ACL (knee ligament) or rotator cuff repairs (shoulder). Many of these surgeries do not have complete success but new biomaterials have the potential to revolutionize soft tissue surgeries. Dr.

Ameer's lab is building ceramic materials to replace older models in orthopedic surgery. These materials can build bone and result in less scar tissue than traditional materials. Northwestern investigators have published dozens of articles on the translational research involved in soft tissue research and developed a compound called Citregen that reduces inflammation and supports the ability to transfer mechanical forces due to its elasticity. This has been shown in a sheep model as well as in the basic science laboratory. Future applications include bone "spacers" and other devices for multiple orthopedic surgery procedures and are on a pathway to FDA approval. Stryker, a larger maker of orthopedic surgery devices, is considering Citregen as an option to repair tendons without as much trauma as traditional approaches.

In summary, we learned a lot about the modern partnerships needed for drug and device delivery and some specific examples of current and future translational science research at Northwestern benefitting human health. For more information, please see the CARE center website: Center for Advanced Regenerative Engineering - Northwestern University

Diane Wayne, MD