Repairing Soft Tissue (Dr. Derwin)

Headlines from the sports world have taught us the words “rotator cuff injury.” The shoulder’s rotator cuff is not one but a group of tendons that coordinate to lift and rotate the arm. If this cuff is torn, simple actions like stretching, lifting, or moving the arm become difficult and a source of disabling pain, reduced shoulder function, and weakness. Such tears affect not only athletes, but 40% or more of patients over age 60, and some 250,000 rotator cuff repairs are performed each year in the US. Even with improvements in our understanding of this condition and advances in surgical treatment, healing this tendon tissue after the cuff is repaired remains a great challenge. Failure rates of 20%-70% for rotator cuff surgery continue to be reported. The reasons why this repair surgery fails are many, based on patient age, size of the tear and how long the tendons have been torn, how much the muscles have weakened and degenerated, tendon quality, the repair technique itself, and whether the patient progresses or not during post-surgical rehabilitation. Our researchers are investigating how to do better.

In the midriff, the abdominal wall is made up of the soft tissues of the outer skin and underlying fatty and fibrous layers. Hernias, in which the intestines push through weakened parts of the abdominal wall, complicate nearly one third of all surgeries in the abdomen, and an estimated 350,000 hernia repairs, costing $3.2 billion, are performed each year in the US alone. The rate of repeat hernias is very high, with 24%-43% of hernia repairs resulting in failure and the return of the hernia. It is estimated that just a 1% reduction in that rate would mean a cost saving of $32 million each year.

Both of these clinical problems require a way to improve repair of the soft tissues involved in the interaction of muscles and skeleton. Currently, various artificial and natural (“synthetic” and “biologic”) materials have been used to construct scaffolds on which cells can grow to repair soft tissue, but such scaffolds have shown only limited success so far. To address this need, researchers at the Cleveland Clinic have been developing new composite scaffold materials, made from biologic and synthetic materials. These high-tech scaffold materials, tested in the laboratory, have shown promise for improving repair of the tendons of the rotator cuff; now they are ready to be tested in human trials. Laboratory research on the use of these new scaffold materials for repair of the abdominal wall and associated hernias is also ongoing. In the future, we expect to adapt these scaffold materials to help regrow soft tissues in skin, skull and facial bones, and genitourinary organs (organs of reproduction and urine elimination).

Summary: Dr. Derwin is developing a novel hybrid biomaterial that is both strong and biocompatible for repair of soft tissues in the shoulder and abdominal wall.

Treatment for Rheumatoid Arthritis (Dr. Calabro)

Rheumatoid arthritis (RA) is a disease affecting the body’s bone joints, often especially joints in the hand, causing them to become inflamed and painful or even to change shape because of swelling and uncontrollable bending of the bones. RA affects more than 70 million people worldwide, and about 2 million people in the US alone. RA is a disabling condition, often deteriorating to bone rubbing against bone; if not adequately treated, RA can lead to complete loss of the ability to move the fingers, hands, hips, and knees. The cause of RA is unknown, and there is no cure. Current therapies for RA can treat only
the symptoms of the disease or can slow down the disease by acting on special “immune cells” in the body, cells that typically fight infection. But treatments for RA that stop immune cell activity or change those cells in some way affect the body’s entire disease-fighting system. Serious long-term side effects often occur, such as life-threatening infections, issues with bleeding or infections throughout the bloodstream, diabetes, cataracts, weight gain, kidney and liver damage, inability to fight off infection, and increased risk of cancer and of death. None of the current treatment options stop RA, so the only option at advanced stages of RA is to have a total joint replacement.

Researchers in BME have discovered a unique protein modification in the joints that binds to, keeps together, and activates the immune cells responsible for RA. These same researchers have discovered that small sugar molecules can be used as a therapy to cleanse the joint of this protein modification; this cleansing process removes the signal that inflames the joints and is the trigger that keeps the RA disease process going. This approach – cutting off the RA signal before it starts doing damage to the joints – has the potential to effectively treat RA without the side effects associated with current therapies.

**Summary:** Dr. Calabro has developed a drug compound that "removes" the cell signal that causes rheumatoid arthritis.

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**Managing Carpal Tunnel Syndrome (Dr. Li)**

The Hand Research Laboratory, led by Dr. Zong-Ming Li, focuses on improving the care and management of carpal tunnel syndrome (CTS). CTS, the most common disorder of muscles and bones of the hand and arms, affect 3%-5% of Americans. Dr. Li and his team use state-of-the-art engineering facilities to research two aspects of CTS: (1) hand function, in terms of hand movements and sensations of touch; and (2) how the carpal tunnel works in relation to its surrounding muscles and nerves. If we can more clearly understand the causes of CTS, we can design ways to improve its diagnosis and treatment, potentially even preventing it. Currently, the laboratory is on the brink of achieving a novel, nonsurgical treatment to relieve CTS symptoms. With additional funding from both private and public sectors, this research could quickly advance to the stage of clinical trials and positively improve patient care.

**Summary:** Dr. Li’s Hand Research Laboratory team has discovered novel approaches that promise to treat carpal tunnel syndrome without the need for major hand surgery.

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**Bone Loss and Delayed Fracture Healing (Dr. Midura)**

In the United States, osteoporosis (“porous bone disease”) will affect 1 in 2 women and 1 in 4 men over a lifetime. Several factors lead to having holes in what should be solid bone: menopause, advanced age, general lack of exercise (being a “couch potato”), lack of use of specific bones (for example, leg bones after long bedrest due to physical illness or injury), long-term steroid use, and any combinations of these causes. Osteoporosis describes a loss of bone tissue, lessening the skeleton’s ability to function, to the extent that “fragility fractures” can occur even while a person is going about normal daily activities; such fractures put the skeleton at risk of even more severe fractures or breaks. To complicate matters for osteoporosis patients, any fractures typically take much longer to properly heal than in age-matched individuals without osteoporosis. Fortunately, several drug and device treatments exist to lessen the bone loss associated with osteoporosis, though only a few of them will actually reverse a state of advanced bone loss and allow the skeleton to function as when the person was younger. We are still trying to understand all the effects of these treatments on the process of bone healing. In our laboratory research program, we are actively studying how (and to what extent) these treatments might reverse bone loss and improve delayed bone healing. Our goal is to rigorously compare how well existing treatments work and find ways to improve fracture healing in our model systems. Our future research goals are to apply our increasing knowledge to patients to develop novel treatments that will prevent osteoporotic fractures by building strong new bone tissue, as well as promote better healing of such fractures.

**Summary:** The Midura laboratory studies the causes and prevention of osteoporosis and seeks to improve the delayed fracture healing responses associated with osteoporosis.