Inspired by mussels, a strong adhesive

Bivalve mollusks, such as the blue mussel *Mytilus edulis*, inhabit coastal waters, attached firmly to rocks and other fixed substrates despite the wet environment and continual, sometimes intense, tidal and wave action. Mussels achieve this remarkable feat by secreting unique protein-based adhesive materials that cement them to their chosen surfaces. These adhesives cure quickly and hold fast, even in wet conditions and on all kinds of surfaces—properties that make them well-suited to myriad clinical applications in addition to their original purpose.

Hemostasis, wound closure and healing, dental and bone repair, tissue engineering, device implantation and drug delivery could all benefit richly from these characteristics. As a result, various researchers have attempted to develop bioadhesives based on mussel adhesive proteins, either by isolating and purifying the natural compounds or by synthesizing their mimics in the lab. Jian Yang (The Pennsylvania State University, University Park, and University of Texas at Arlington) and colleagues took the latter

approach and now report the creation of injectable citrate-based mussel-inspired bioadhesives (iCMBAs) and the successful use of these synthetic polymers in wound-healing studies in rats.

Wet adhesion strength was 2.5–8 times stronger for iCMBAs than for fibrin glue, a tissue adhesive often used in clinical hemostasis. The iCMBAs also had controlled biodegradability, mechanical properties similar to those of tissue and very high cell and tissue compatibility *in vitro* and *in vivo*. They stopped bleeding instantly without the need for sutures and successfully closed relatively large incision wounds (2 cm long × 0.5 cm deep) on the dorsum of Sprague-Dawley rats within 2 minutes, a result that cannot be accomplished with fibrin glue. Furthermore, iCMBAs accelerated wound healing and were completely degraded and absorbed within 28 days without provoking an excessive inflammatory response (*Biomaterials* 33, 7972–7983; 2012).

The results suggest that iCMBAs are suitable candidates for biological and surgical applications including wound

closure; tissue grafts (e.g., for hernias, ulcers or burns); hemostasis; sealing of vascular anastomoses; and treatment of gastrointestinal fistulas, leaks, bleeding or perforation. “There are so many applications that you can use this glue for to help in surgery,” Yang noted in a press release.

Yang and his colleagues plan to improve the iCMA formula. “We are still optimizing our formulation. We are still trying to make the adhesion strength even stronger. We can introduce another component with antimicrobial properties, so it can do two functions at once,” stated Yang.

Monica Harrington

RAT BULLIES: A RECIPE FOR AGGRESSION

Epidemiological studies have shown that early exposure to trauma, particularly fear and maltreatment, strongly increases the likelihood of violent behaviors developing later in life. Despite the clear connection between adolescent adversity and adult aggression, the neurobiological mechanism behind this association remains unclear. In a study published in *Translational Psychiatry* (published online 15 January 2013; doi:10.1038/tp.2012.144), researchers at the Brain Mind Institute in Lausanne (Switzerland) report they have developed an animal model for pathological aggression induced by peripubertal exposure to stress and that their findings mirror those described in humans.

Lead researcher Carmen Sandi and her team placed 28- to 42-day-old adolescent rats on an elevated platform under bright lights and/or exposed them to fox odor for 25 minutes a day for 7 days. They observed that rats exposed to this stress protocol displayed extreme violent and aggressive behavior, as adults, toward any new rat placed in their cage. Control rats not subject to the fearful stimuli as adolescents were significantly less likely to attack intruders during adulthood.

Furthermore, the tormented adolescent rats exhibited hyperactivity in the amygdala, the structure in the brain associated with fear, and showed hypoactivation of the medial orbitofrontal cortex; the area of the brain involved in the cognitive processing of decision making. Both of these brain activity patterns have been linked to violence and aggression in humans. Additionally, the stressed adolescent rats presented anxiety and depression-like symptoms and had higher testosterone and lower corticosterone levels. These factors are also associated with increased violence and aggression in humans.

Finally, peripubertal stress appeared to affect the rats on a genetic level, causing epigenetic changes in the prefrontal cortex by increasing the gene expression of monoamine oxidase A (MAOA), which led to the escalated production of the enzyme, known to break down serotonin. Remarkably, treatment with an MAOA inhibitor during adulthood reversed the adolescent stress-induced aggressive behavior.

The stress protocol failed to provoke similar behavior changes when performed on adult rats, suggesting that adversity experienced in adolescence, but not in adulthood, can severely alter neural and physiological programming, thus increasing one's proclivity for violence later in life. This study provides a novel animal model upon which future research on the effects of early life trauma can be built.

Thomas Rowley