Design Article

Accelerated Coagulation Process

Cathy Cheng, Allecia Dodd-Noble, Mitali Gupte, Kaby Maheswaran, Suren Maheswaran, Hannah Shell
Andover High School, Andover, MA

Reviewed on 28 April 2018; Accepted on 19 May 2018; Published on 22 October 2018

We constantly receive numerous minor injuries like paper cuts or scrapes in our everyday lives. The healing process of the majority of these minor injuries starts with the coagulation process, or the process of stopping bleeding through blood clots. However, sometimes, we do not have time to treat even minor injuries, and these injuries can take days or weeks to heal. We are proposing a topical spray that would accelerate the coagulation process when applied to the wound immediately upon bleeding. We would use the F-gene series, a series of genes that creates the proteins needed in the coagulation process, to produce these proteins in the *Escherichia coli*.

Keywords: Minor wounds, coagulation, treat, healing, coagulation cascade process, synthetic biology, wounds

Mentors: Lindsey L'Ecuyer*, Emily Thomas - Authors are listed in alphabetical order.
Please direct all correspondence to: *LLecuyer@aps1.net

Background

Wounds occur often in our lives. As technology and medicine have evolved, so too have healing methods. Since the invention of the Band-Aid in 1920, wound healing has come a long way. With the number of injuries, however minor, a person receives in their lifetime, such occurrences become major inconveniences over time. With the aid of modern science and technology, the prospect of accelerating the natural healing process has come into play. Different individuals and companies have stepped up to address the problem, however, each brings a different solution to the table. Some choose to focus on chronic wounds, others concentrate on different stages of the healing process, and still others pinpoint different approaches altogether.

Many studies have chosen to address chronic wounds, which are wounds that take longer than three months to heal. A number of groups, including those at Uppsala University in Sweden and other research groups in Europe, have taken this route. At Uppsala, lactic acid bacteria are being used to help deliver chemokine to chronic injuries. In other places in Europe, scientists are investigating the role of flavonoids, which belongs to a class of plant pigments, as a means of strengthening veins. However, these compounds are primarily used on infected wounds, and research has yet to prove their effectiveness on clean wounds. In both European cases, the decision to manage chronic wounds poses barriers against a market that may require targeting more minor injuries.

Other studies concentrate on different stages of the healing process. At the University of Zurich, a team has developed an idea to use nerve cells called glial cells to allow new layers of skin to form. With this method, Zurich is focusing on the later steps of the wound healing process. Similar to the work performed at Uppsala University, scientists at Zurich focused too on chronic wounds.

For our project, however, we decided to address more minor injuries. This way, our product will likely be more accessible to the average person. We are also planning on targeting the earlier stages of the healing process. The entire process is made up of three or four phases, with the variation depending on different authors. Though each has its own characteristics, these phases often overlap. When divided into four phases, they are the hemostasis phase, the inflammatory phase, the proliferation phase, and the remodeling phase. At the University of Zurich, scientists focused on the remodeling phase as well as the later parts of the proliferation phase. For our project, we will focus on the inflammatory phase, which contains the coagulation cascade process. This process, however, starts during the hemostasis phase as well. By targeting the earlier phases, we will

enable the body to address the presence of the wound faster, so that the process may carry into the later phases quicker.

Systems Level

Our system is designed to accelerate the natural healing process. Utilizing a chassis, we will produce the F-gene series proteins. For our research, we took a look at the F3, F5, and F10 genes, although there are many more involved. Each codes for coagulation factors which play a role in the coagulation cascade process. In this process, a series of chemical reactions activates a prothrombin activator, which then converts the prothrombin into its active form, called thrombin. Once this has been achieved, the thrombin forms the blood clot to stop the bleeding. After the conversion of prothrombin to thrombin, we plan to purify the product from the chassis, and form it into a topical spray to be used on minor injuries.

Device Level

Escherichia coli will be used as our chassis to produce the proteins needed to accelerate coagulation and begin the healing process. *E. coli* is a gram negative bacteria and ideal for the use of synthetic biology. This bacteria has a rapid doubling time of less than an hour and will help grow saturated strains overnight. Also, as *E. coli* cannot survive in the intestines, it is safe to use in the laboratory. The *E. coli* will be used to produce the F-gene series proteins, which will then be extracted. We have not decided which specific strain of *E. coli* we will use.

Parts Level

For a system, various parts are necessary. In this project we have a promoter, terminator, ribosome binding site, coding sequence, inducer, and a regulatory encoder. For our promoter, we are planning to use a cell signaling promoter. The terminator we plan on using is the BBa_K801012 from the iGEM registry. The BBa_B0030 will be used as our ribosome binding site which will be modified from R. Weiss. Our coding sequence is the F-gene series, which is responsible for creating blood clotting factors that lead to the coagulation cascade process. We have much more to research about our project and hope to finish researching by the end of next year. We are in the process of searching for an inducer and a regulatory encoder to better serve the needs of our project.

Safety and Discussion

As with any other project in synthetic biology, our project brings up concerns of biosafety. With our project, we plan to accelerate the natural healing process. As our design involves a topical spray, this generates questions over possible infection as a result of our spray, especially as we will be using *E. coli* as the chassis to produce our product. However, given that we will carefully extract our product from the chassis, there will be no concerns with contamination. Through our project, we wish to promote both the knowledge of synthetic biology as well as biosafety. Although the usage of bacteria on open wounds can be concerning to the public, our goal is to make the process of our product clear, so as not to cause concerns. We have just begun researching the introduction parts of this project. There is much more to discover and clarify before we can put this idea into action.

Going into the future, we want to direct the application of our product towards hemophilic patients. We also want to create different degrees of our product for the various needs of common wounds. Although minor, everyday wounds are common; there is a call for solutions to chronic or major injuries. The process of healing for chronic injuries is much different; however, our research could be a foundation for our project. We will begin our investigation into accelerating the natural healing process by focusing on everyday injuries; however, we believe our product has hope for improvement and expansion in the future to serve the needs of a wider market.

Acknowledgements

Our team at Andover High School would like to express our gratitude and acknowledgements for several people, without whom this project would not have been possible. First of all, we would like to thank Mrs. L'Ecuyer for giving us the encouragement and help every step of the way, from getting to understand synthetic biology in the very beginning, to developing and finalizing our design for our product. We would also like to thank our mentor, Ms. Thomas, for her guidance as we were in the process of formulating a direction in which to take our designs. Next, we would like to thank Dr. Kudell for creating the BioBuilder program and allowing us to explore our passions as well as the field of synthetic biology, and for giving us the opportunity to create and design this project. We could not have done any of this without the help from everyone involved.

References

Fung B. Infographic: The Average Person Gets 9,672 Minor Injuries in a Lifetime. 2012 May. Retrieved March 11, 2018, from https://bit.ly/2xMLqUe

Gj G. Follow. Blood coagulation. 2015 May. Retrieved March 11, 2018, from https://bit.ly/2xXgxM0

Life Enhancement Products, Inc. Accelerated Wound Healing with Flavonoids. 2001 Jun. Retrieved from https://bit.ly/2y2Ls9Y

Logarta M. Scientists discover gene for advanced healing and limb regeneration. 2013 Nov. Retrieved March 11, 2018, From https://bit.ly/2ItVVjt

Maynard J. How Wounds Heal: The 4 Main Phases of Wound Healing. 2017 Jul. Retrieved March 11, 2018, from https://bit.ly/2x36ftl

National Library of Medicine. F5 gene - Genetics Home Reference. n.d. Retrieved March 11, 2018, from https://bit.ly/2y1seS0

National Library of Medicine. F10 gene - Genetics Home Reference. n.d. Retrieved March 11, 2018, from https://bit.ly/2Ncbzkb

UniProt Consortium. European Bioinformatics Institute Protein Information Resource SIB Swiss Institute of Bioinformatics. 2018 Feb. Tissue factor. Retrieved March 11, 2018, from https://bit.ly/2y4Ehhm

University of Zurich. Unexpected helpers in wound healing. 2018 Ja. Retrieved from https://bit.ly/2RdtMkM

Uppsala University. New technology for accelerated wound healing discovered. 2018 Feb. Retrieved from https://bit.ly/2FOtREX