Environmental Analysis

Introduction

Collagen is a protein, popular due to its ability to be applied for many uses. In the food industry, collagen's properties, such as high protein content and the ability to absorb water make it appealing. Specifically in the biomedical and the pharmaceutical field, collagen is used to carry genes, proteins, and drugs, as well as serving as a replacement for human skin. Recently, collagen has been produced by extracting the protein from animals, which can be a task that requires a lot of time and money, along with involving inhumane practices.

Project Description

Team CCA San Diego's study is to produce collagen using S. Cerevisiae expressing scl1, a bacterial protein that closely resembles human Type 1α collagen.

Bacterial collagen is used instead of recombinant human collagen because they do not require the expression of hydroxylase enzymes that would add cost on a large-production scale, while still maintaining remarkable similarities to human collagen. The resulting product will potentially be combined with sericin for structural and functional support, cross-linked via UV radiation, and spun to form thread. The final product will be an engineered bio fabricated collagen, cross-linked with sericin to create thread that can be used for biomedical purposes such as sutures, membranes, or thread.

Existing Problems with Current Solutions

Collagen's popularity has increased due to its qualities that are helpful in the food, cosmetic, and biomedical pharmaceutical industries.

In animals, collagen can be extracted from the skin, tendons, and bones; nevertheless, the amount of collagen found varies based on different factors of the animal. The species of animal and physical features like body weight and hooves are all factors that influence the yield of by-products of an animal when the animal is slaughtered. The by-products of animal slaughter are generally what collagen is found in, but due to the physical differences mentioned, there is a range for the yield of by-products in different animals. For cattle, pigs, and sheep, there is a 10%-30% yield of by-products, and a

5%-6% yield of by-products in poultry. Especially since collagen is growing its popularity in the cosmetic, pharmaceutical, and culinary industries, the desire to extract or produce collagen has increased, and there will be more incentive to extract collagen from animals. However, to slaughter many animals with only about 5%-30% of that animal being useful to extract collagen is inhumane. Some of those by-products will not even contain collagen, making the amount of collagen produced seem miniscule from slaughtering an animal. The by-products that do not contain collagen sometimes have other purposes -- some being edible -- but the by-products that do not have any use are discarded, and the waste accumulates.

Cows and pigs are the two main animals slaughtered to extract collagen. The process of killing large amounts of cows is difficult to see as ethical as in some cases, parades of cows are led to a chamber where they are zapped unconscious and then killed in a routine like an assembly line. Specifically when there is a desire to extract a large amount of collagen from cows and pigs, there would be a need to slaughter a large group of animals.

Another problem of using animals to obtain collagen is that there is a possibility that using collagen extracted from animals has a potential of spreading diseases, as well as allergic reactions. Bovine spongiform encephalopathy, or “mad cow disease”, and foot and mouth are two diseases that could potentially be transmitted two humans through animal extracted collagen. Collagen from animals can also cause prions to be spread to human cells. Prions are a type of protein that can cause normally folded proteins to fold abnormally, which causes damage to the brain. There is a lot of variation in the preparation of collagen extracted from animals that could spread diseases as well. Because of the variabilities in animal extracted collagen, the collagen is inefficient, and not preferable when there are large amounts of collagens that vary. Currently, the common method of producing collagen is expensive and not time efficient.

Therefore, Team CCA San Diego’s solution to the problem of using collagen extracted from animals is to use bioengineered collagen, which will be more efficient (with less variability), better humane practices, and ease the worry of spreading animal related diseases. Bioengineering collagen instead of obtaining the collagen from animals would also take less time. To extract collagen from animals, the animal (most commonly either a pig or a cow) would need to be processed, involving its steps to be killed, and then separating by-products that contain collagen and other by-products that do not. Parts of the animal like hooves or horns would need to be removed, and then the overall process of extracting collagen from the animal carcass would require more time than bioengineering the collagen.

Once our team has bioengineered the collagen, it will be used to produce a thread where it will go on to be used in biomedical applications.

Potential problems with our project + what we fixed with existing solutions

One of the potential problems with our project is that we had planned to use yeast in order to express the collagen, but yeast, through research, has not been an effective tool. Plasmids will be used in an attempt to fix this problem.

Scl1, the bacterial protein that will be used in our project, has the possibility of spreading sickness because it comes from bacteria. Luckily, it is an unlikely occasion and therefore there is a very small chance that sickness would spread. Similarly, the bacterial proteins could be absorbed and then cause prion disease; luckily, it as well has a small chance of occurring.

Furthermore, the bacteria that our team would use to produce collagen has an unlikely chance of mutating and creating a supervirus. If this were to occur, our team would create a killswitch where a piece of the DNA (by exposure by sunlight or not enough food) will cause the bacteria to die.

What we are trying to fix with lab, modeling, and scicomm to address the problems

To address the problem regarding the fact that yeast is not a viable option in being able to express the collagen, we will use plasmids to extract the collagen from the yeast, which has been shown through research to have a much higher success and yield rate of collagen than when simply yeast is used to extract the collagen.

Bioengineering collagen takes more time and is more expensive than simply extracting collagen from animals unfortunately. CCA San Diego iGEM is still currently finding a solution to make the bioengineering process more affordable and quick to make because even though bioengineering the collagen is much more environmentally friendly and kind to the environment, many companies and factories primarily care a mass producing and manufacturing collagen to make it more accessible.

An issue is that manufacturers are more concerned with making money than using a safe, and overall advantageous way of making collagen. This means that manufacturers may be hesitant to choose to switch from extracting collagen from animal parts and deceased humans to bioengineering it which

takes more time but is safer. Due to this unforeseen issue, it is important that people take the time to explain specific features of the project in order to convince people to switch while still being conscious and simple so that people can quickly and effectively see the benefits of bioengineered, safe collagen to randomized extracted collagen.

Concept Selection matrix for different aspects of bioengineering collagen and naturally extracting collagen from animals

	Extracting collagen from animals	**Bioengineering collagen**
Humane practices	No, extracting collagen from animals is not humane at all and is far less humane than bioengineering collagen, like our project topic. In order to gain a large amount of collagen to be applied to biomedical purposes, a large amount of animals would have to be killed as the yield of by-products is low and only a portion of those by-products contain collagen.	Yes, bioengineering collagen is more humane than extracting collagen from animals. Since we are bioengineering collagen and do not need to kill animals (mostly pigs and cows), the production of bioengineered collagen will be completely humane.
Time (how long the process of extracting collagen takes)	Extracting collagen from animal hooves and other parts and humans is the most time efficient as it would require time to kill the animal, gather the by-products, determine which of the by-products contain collagen, and prepare the collagen.	Bioengineering collagen is more time efficient than extracting collagen from animals because bioengineering methods will be utilized which will produce the collagen itself. Taking steps to prepare the animal will not be needed.
Efficiency/effectiveness	The process is not very	More efficient and

	efficient or effective. Variability in preparation of the collagen extracted from animals can lead to difficulties. Animal extracted collagen can transmit diseases, as well as some people may experience allergic reactions to animal extracted collagen. The yield also depends on the species of animal, and on physical properties of the animal itself.	effective. Since bioengineered collagen will be manufactured in a lab and will be able to be controlled.
Consistency	This method of extracting collagen from animals and humans is not very consistent. The specific types of collagen can slightly vary from species to species and sources in general. This creates some problems in the engineering process of making things out of collagen currently since each type is slightly different at the molecular level so they all react in different ways.	The process of bioengineering collagen is more consistent than naturally extracting collagen from species of animals and different sources. Since bioengineered collagen is more monitored in the engineering process and follows strict lab protocol, all of the bioengineered collagen will be exactly the same at a molecular level meaning that there will be fewer, if any, variations in how the collagen reacts with things. To conclude, bioengineering collagen would give the collagen a more consistent finish with fewer variations of the same thing.
Waste	Extracting collagen from	Bioengineering collagen

	animal species and humans creates a great deal of waste since the animals must essentially be dissected to an extremely small scale in order to extract the collagen from them and the remains of the different animal species, and sometimes humans, are left without a use so they create waste.	in a lab would create less hazardous waste for the environment. This is due to the fact that there are fewer items and parts that cannot be used and only classic lab waste is left while mutilated and dissected animals are left in the process that is used currently, extracting it from dead animal species and humans.
Biomaterial use	When extracting collagen from animals and humans, the collagen cannot be used to deliver drugs or develop the bioengineering of human tissue. It is not heavily regulated and the molecular structure cannot be controlled when using the method which simply extracts collagen from animals.	Biomedical engineering collagen in a lab rather than extracting the collagen from animals means that the collagen which is biomedically engineered can be used to deliver drugs to various parts of the body and more. Since the lab procedures are much more regulated than the current method, which is extracting collagen from deceased animals and humans, the molecular structures of each collagen molecule will be much more similar to each other so they can perfectly be recreated every time in order to gie drugs to people. Additionally, bioengineered collagen can be used to create fake human tissue which can be used on any part of the body.

Ability to be manipulated	Since this process of extracting the collagen from animals simply extracts the collagen, the specific structure of the collagen is already predetermined and cannot be manipulated into being used for a certain or specific cause that it may be needed for.	Bioengineering collagen creates the collagen from yeast from scratch, or the very beginning of the process. This is advantageous because it can be manipulated in a large variety of ways throughout the entire experiment to be suited for the specific cause or purpose that people want to use the bioengineered collagen for and people can use it for so many things if it is slightly modified including tissue development, as well as being a drug deliverer. Different drugs could be delivered based on how the collagen structure is modified during the bioengineering process.