

Royal Jelly Shows Promise in Assisting Stem Cell Research

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STORY AT-A-GLANCE

- › Stanford University scientists found royalactin, a protein found in royal jelly responsible for the queen bee's massive growth, has the ability to keep mouse embryonic stem cells pluripotent by inhibiting differentiation
- › Stem cells are pluripotential, meaning that they have the ability to turn into any and every type of tissue to form an entire being, be it animal or human
- › They also identified a protein with similar qualities found in mammals, dubbed Regina, which like royalactin allows embryonic stem cells to maintain their naïve state
- › Embryonic stem cells have a tendency to differentiate into mature tissue cells when grown in the lab, and in order to use the stem cells for research and/or therapies, they must be kept in their "naïve" state long enough
- › These initial findings could eventually lead to the development of drugs to boost stem cells in the human body, allowing for the regeneration of healthy tissue in damaged organs

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Aside from being vital pollinators, bees produce a number of products that benefit human health. Honey¹ is an obvious one, but there are others as well, such as royal jelly, a nutritious substance secreted by nurse bees as exclusive nourishment for the queen of the hive.

Research^{2,3,4} by Stanford University scientists found royalactin (also known as major royal jelly protein 1, or MRJP1), a protein found in royal jelly responsible for the queen's massive growth, has the ability to keep embryonic stem cells pluripotent.

This initial finding could eventually lead to the development of drugs to boost stem cells in the human body, allowing for the regeneration of healthy tissue in damaged organs, be it your heart, eyes, skin or spinal cord.

They also identified a protein with similar qualities found in mammals, which they dubbed Regina – a nod to the queen bee for which royalactin is made – which like royalactin allows embryonic stem cells to maintain their naïve state. According to the authors:

"This reveals an important innate program for stem cell self-renewal with broad implications in understanding the molecular regulation of stem cell fate across species."

Researchers Discover Program for Stem Cell Self-Renewal

Embryonic stem cells are the product of the initial meeting of egg and sperm. Three days after fertilization of the egg, an inner cell mass can be isolated, and these are the embryonic stem cells that, if left alone, will grow into a fetus.

Stem cells are pluripotential, meaning that they have the ability to turn into any and every type of tissue to form an entire being, be it animal or human. Adult stem cells, in contrast, are multipotential, meaning they only have the ability to form subsets of tissue.

The problem researchers have is that embryonic stem cells have a tendency to differentiate into mature tissue cells of various kinds when grown in the lab, and in order to use the stem cells for research and/or therapies, they must be kept in their "naïve" state long enough. As explained by New Atlas:⁵

"With the ability to differentiate into all kinds of cells that serve specialized functions, like muscle cells, red blood cells or brain cells, embryonic stem cells

have incredible potential. But growing them in the laboratory is difficult, because their natural inclination is to quickly outgrow their pluripotent state and become something else.

To preserve that pluripotency, scientists must add special molecules to the culture that inhibit that behavior. Wang and his team found that by adding royalactin instead, they could stop the embryonic stem cells from differentiating just as well.

In fact, they found that they were able to maintain the cells in their embryonic state for up to 20 generations in culture without the need for inhibitors."

This was a complete surprise. Normally, scientists must use leukemia inhibitor factor to prevent the embryonic stem cells from differentiating when grown in culture. What they discovered is that royalactin performed the same function. The question is: How?

Royalactin-Like Protein Inhibits Embryonic Stem Cells

Mammals do not produce the royalactin protein, yet the royalactin activated a network of genes known to code proteins that allow the embryonic stem cells to maintain their pluripotency. To find the answer, the researchers searched scientific databases to identify human proteins with structures similar to that of royalactin.

What they found was a protein known as NHL repeat-containing-3 protein or NHLRC3, produced during the development of the mammalian (including human) embryo. They then duplicated the mouse experiment using NHLRC3, which was found to trigger a similar gene network as royalactin.

The end result was the same – the embryonic stem cells maintained their pluripotency in culture. Kevin Wang, assistant professor of dermatology and lead author of the study, commented on the results, saying:⁶

"It's fascinating. Our experiments imply Regina is an important molecule governing pluripotency and the production of progenitor cells that give rise to

the tissues of the embryo. We've connected something mythical to something real."

Next, Wang and his team will investigate whether Regina – the mammalian equivalent of royalactin – has the ability to affect cell regeneration and wound healing in adult animals. And, as reported by New Atlas:⁷

"It could be used as another way to keep embryonic stem cells pluripotent in the lab, and could one day lead to the development of synthetic versions that deliver stocks of stem cells in the human body.

[T]hose kinds of drugs could be used for all kinds of things, from generating healthy tissue for damaged hearts, degenerating eyes, injured spinal cords and severe burns."

What Is Royal Jelly and How Is It Made?

Royal jelly is a gelatinous, milky substance secreted by the hypopharyngeal and mandibular glands of worker honeybees between the sixth and twelfth days of their life,⁸ and is an essential food for the development of the queen bee. It's a complex substance containing proteins (12 to 15%), sugars (10 to 12%), fat lipids (3 to 7%), along with a variety of amino acids, vitamins and minerals.⁹

Compared with the short-lived and infertile worker bees, the queen bee, which is exclusively fed royal jelly, is characterized by her extended lifespan and her well-developed gonads. Therefore, royal jelly has been long-used as a supplement for nutrition, antiaging or infertility.

The larva selected to become queen is fed royal jelly exclusively, while the rest of the larva receive royal jelly along with pollen and honey. Research^{10,11} reveals this exclusive royal jelly diet activates certain genes in the queen bee, allowing her to grow much larger and become such a prolific egg layer. The honey and beebread fed to worker bee larvae contains p-coumaric acid, and it's the presence or absence of p-coumaric acid that determines the caste of the bee.

Larvae fed royal jelly to which p-coumaric acid had been added produced adults with reduced ovary development. "Thus, consuming royal jelly exclusively not only enriches the diet of the queen-destined larvae, but also may protect them from inhibitory effects of phytochemicals present in the honey and beebread fed to worker-destined larvae," the researchers explain.¹²

Health Benefits of Royal Jelly

Folklore in Europe and Asia has it that royal jelly is a powerful rejuvenator capable of boosting longevity and fertility. It's also been used to promote hair growth and minimize wrinkles. In Chinese medicine, royal jelly is revered as a substance that helps increase life expectancy, prevent disease and restore youth.

The fact that the protein Regina in mammals and humans appears to work like royalactin in royal jelly could possibly account for some of these benefits. Royal jelly also has antimicrobial benefits, courtesy of bee defensin-1, an antimicrobial peptide found in it. Because of components such as these, it's fair to assume that royal jelly is in fact beneficial for humans.

That said, the idea that consuming royal jelly might somehow affect your stem cells is probably taking things too far. There's no evidence of that – only that royalactin allows mammalian embryonic stem cells in an undifferentiated state in a lab environment.

Also keep in mind that it's difficult to ensure potency and quality of royal jelly products on the market. Toxicology tests suggest most if not all honeys, for example, are tainted with the herbicide glyphosate, and the bee population has taken a hit around the world due to various pesticide exposures. If the bees have toxins in them, it's feasible their royal jelly might be contaminated as well.

Still, the research was conducted by a very prestigious institution and published in a respectable journal, and they seem to believe there are possibilities here. Just realize that the focus is on Regina, the mammalian protein equivalent of royalactin, and not on royal jelly itself.

Health Benefits of Bee Propolis

Propolis is yet another bee product with health benefits, including immune-boosting properties and strengthening your body's defenses against bacteria, viruses and other disease-causing organisms.

Propolis is used by bees to close openings in their beehives, which is why it is also referred to as "bee glue." The materials are usually taken from leaves, bark, flower buds and other plant parts. These are then combined with bee saliva, wax and pollen, which are then adhered to the hive holes.

Studies suggest propolis also protects the bees from bacterial infections and possible external elements that may endanger the whole colony. In some cases, propolis may also be used to encase the carcasses of hive intruders to stop bacteria from spreading.¹³

Propolis has been used for years in folk medicine because of its proposed effect on various body systems, dating back to the time of the ancient Greeks, Romans and Egyptians.

In fact, Hippocrates notes that propolis is beneficial for promoting wound healing, both internal and external, while Pliny the Elder documents that propolis may be used to treat tumors, muscle pain and ulcers. This bee product was also documented in the Persian manuscripts as a remedy for various conditions, including eczema and rheumatism.¹⁴

Today, propolis is used in a wide variety of skin care products, including creams and extracts to promote wound healing and ease various types of infections. It is also available as a supplement, with people taking it on a regular basis to boost their immune system function.¹⁵

Propolis Has Flavonol With Health Benefits

Research also suggests a flavanol in propolis called galangin has anticancer effects on several cancers, including melanoma, hepatoma, leukemia and colon cancer.

In one such study,¹⁶ galangin was found to induce apoptosis (programmed cell death) in two types of colon cancer cells (HCT-15 and HT-29 specifically), and that the effect killed the cancer cells in a dose-dependent manner. According to the authors:

"We also determined that galangin increased the activation of caspase-3 and -9, and release of apoptosis inducing factor from the mitochondria into the cytoplasm by Western blot analysis.

In addition, galangin induced human colon cancer cell death through the alteration of mitochondria membrane potential and dysfunction. These results suggest that galangin induces apoptosis of HCT-15 and HT-29 human colon cancer cells and may prove useful in the development of therapeutic agents for human colon cancer."

Galangin has also been shown to inhibit inflammation by regulating the nuclear factor-kappa B (NF- κ B), PI3K/Akt and peroxisome proliferator activated receptor- γ (PPAR γ) signaling in activated microglia in the brain and thus should improve or prevent Alzheimer's.¹⁷ Additionally, galangin reduces insulin resistance by increasing the activity of hexokinase and pyruvate kinase, promoting glucose consumption and glycogen synthesis.¹⁸

Royal Jelly May Be Beneficial, but Don't Expect Miracles

In summary, while royal jelly has a number of health benefits, it's premature to assume it can affect your stem cells directly. A number of studies done on royal jelly have focused on its potential effects on cancer, fertility and its role in testosterone production.

In one study,¹⁹ infertile men were given different dosages of royal jelly and honey to increase the production of testosterone. After three months, those given royal jelly had higher testosterone levels, improved sperm active motility and luteinizing hormone levels, thus showing the potential impact royal jelly can have on infertility in men.

In another study,²⁰ royal jelly was found to reduce symptoms of mucositis in patients suffering from neck and head cancer. Mucositis refers to the inflammation of the

digestive tract brought on by chemotherapy and radiotherapy. Patients who were given royal jelly thrice a day showed a decreased occurrence of mucositis.

A study²¹ published in an obscure Chinese journal also suggests royal jelly has an antisenescence effect on human lung fibroblasts in cell cultures. Other studies have found royal jelly supplementation can improve menopausal symptoms²² and Type 2 diabetes outcomes.^{23,24}

How to Identify a Quality Product

So, provided you can find a high-quality product (which can be expensive), it could be a valuable supplement in some instances. In terms of what to look for when shopping for a royal jelly product, here are a few pointers:

- Fresh royal jelly is ideal if you can find it, but lyophilized royal jelly is also a good and more convenient option
- To assess quality, look for 10-hydroxydecanoic acid (10-HDA) content. Most companies that care about quality will test their royal jelly for this. For fresh royal jelly the typical range is ~1.5 to 2.3%. For lyophilized royal jelly, it is ~4.5 to 6.6%
- Look for organic royal jelly as it is less likely to contain antibiotics or be adulterated

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