

Athena scientists found a way to produce industrial quantities of useful natural compounds by growing them in tomatoes

A super tomato as powerful as 50 bottles of red wine

Given the opportunity to drink fifty bottles of wine or eat one tomato, which would you choose? Scientists at the John Innes Centre have found a way to produce industrial quantities of useful natural compounds efficiently, by growing them in tomatoes.

The compounds are phenylpropanoids like Resveratrol, the compound found in wine which has been reported to extend lifespan in animal studies, and Genistein, the compound found in soybean which has been suggested to play a role in prevention of steroid-hormone related cancers, particularly breast cancer.

As a result of the research led by Dr Yang Zhang and Dr Eugenio Butelli working in Professor Cathie Martin's lab at the John Innes Centre, one tomato can produce the same quantity of Resveratrol as exists in 50 bottles of red wine. One tomato has also produced the amount of Genistein found in 2.5kg of tofu.

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Final meeting at EXPO time: partners join the global enthusiasm for food and nutrition



Milan was chosen as the venue of the final Athena meeting in line with the global feeling on the crucial importance of food and nutrition this year.

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Purple flour against breast cancer



Breast cancer: purple flour against skin damage

The human trial has been conducted within women receiving radiotherapy after surgery for breast cancer



Maria Benedetta Donati

Improving health with proper nutrition is presently considered one of the main goals of biomedical research. In this context, considering the increased impact of cardiovascular and neurodegenerative diseases, the promotion of prevention strategies is essential not only for individuals, but also for health systems in order to reduce the economic burden of chronic diseases.

Food and prevention are closely associated, especially when we talk about the Mediterranean diet. Antioxidants, substances that are found in many of the Mediterranean foods, are among the most important compounds helping the body.

“They are capable of neutralizing the cell damage due to oxidation processes, the result of biochemical reactions in the body. - Explains Professor Maria Benedetta Donati of the Department of Epidemiology and Prevention IRCCS Neuromed, Pozzilli, Italy - These oxidation processes lead to inflammation and tissue aging. It is said, almost jokingly, that the aging of cells is a gradual process of rancidity due to the accumulation of oxidative damage. Any method capable of preventing this process can therefore reduce aging”.

Antioxidants are increasingly the target of studies in the prevention of several chronic degenerative diseases, including neurodegenerative disorders.” More and more - Donati continues - it is widely recognized that vascular and neurological degenerative diseases have a common basis, common cellular processes in which oxidation plays a role. According to recent evidences, in some forms of dementia, such as Alzheimer’s and Parkinson’s disease, a diet rich in antioxidants can prevent, or delay, the progression of cognitive impairment. Moreover, oxidative stress is accentuated in ischemic cardiovascular diseases as a result of the shortage of blood supply in the affected areas”. Flavonoids are among the most active natural antioxidant compounds. Over 4,000 of them are known, present in various foods. They are responsible, in large part, for the characteristic colors of plants, flowers and of some fruits. Now medical research is turning to

these compounds with the hope of discovering new tools for diseases prevention.

IRCCS Neuromed Pozzilli is engaged on this front with the European ATHENA Project, an international collaboration among different research institutes, which share an interest for the study of these particular substances with a specific focus on anthocyanins. They are contained in many foods, especially in Sicilian blood oranges, blueberries, berries of currants, raspberries and eggplant. Red and blue are the colors that characterize foods rich in anthocyanins.

“Among the most interesting experimental results already obtained within the ATHENA project, we can mention the association, in experimental models, between anthocyanins intake and longevity or protection from metabolic disorders. - explains Donati - . Very interesting data were obtained, in addition, on the extension of the area of an experimental myocardial infarction. Indeed, in animals (rats) fed a diet enriched in anthocyanins the tissue damage around the ischemic injury was markedly reduced in comparison with controls; as if there was a reinforcement of defense mechanisms allowing the healthy tissue surrounding the ischemic insult to react”.

Coming to normal eating habits in humans, ATHENA researchers found that consumption of blood orange juice reduces oxidative stress in patients with metabolic disorders, protects DNA from oxidative damage and may reduce cardiovascular risk factors to the same extent, as other anthocyanin-rich foods (fruits and vegetables).

Athena has set one of the biggest human studies on anthocyanins and health.

The human trial has been conducted within women receiving radiotherapy after surgery for breast cancer.

Among side effects, this treatment can cause skin inflammations both short and long term. In these conditions it is not always possible to follow a certain type of diet due to the interference caused by radio and chemotherapy treatments.

Researchers from the Athena study have then tried to enhance the defensive potential of these people through dietary supplementation of a special flour obtained from the cob of a new purple corn specifically developed within the project. This high anthocyanin-rich supplement during radiotherapy should limit the side effects of radiation on the skin.

The skin-damage is detected by a cutometer, a sensitive device able to measure the magnitude of the damage provoked on the skin by radiation.

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Drs Zhang and Butelli have been studying the effect of a protein called AtMYB12 which is found in *Arabidopsis thaliana*, a plant found in most UK gardens and used as a model plant in scientific investigation.

The protein AtMYB12 activates a broad set of genes involved in metabolic pathways responsible for producing natural compounds of use to the plant. The protein acts a bit like a tap to increase or reduce the production of natural compounds depending on how much of the protein is present.

What was interesting about the effect of introducing this protein into a tomato plant was how it acted to both increase the capacity of the plant to produce natural compounds (by activating phenylpropanoid production) and to influence the amount of energy and carbon the plant dedicated to producing these natural compounds. In response to the influence of the *atmyb12* protein, tomato plants began to create more phenylpropanoids and flavanoids and to devote more of energy to doing this in fruit.

Introducing both AtMYB12 and genes from plants encoding enzymes specific for making Resveratrol in grape and Genistein in legumes, resulted in tomatoes that could produce as much as 80mg of novel compound per gram of dry weight – demonstrating that industrial scale up is possible. Tomatoes are a high yielding crop – producing between 50 and 100 tonnes per hectare – and require relatively few inputs, therefore production of valuable compounds like Resveratrol or Genistein in tomatoes could be a more economical way of producing them than relying on artificial synthesis in a lab or extracting them in tiny quantities from traditional plant sources (e.g., grapes, soybeans, etc.).

The tomatoes can be harvested and juiced and the valuable compounds can be extracted from the juice. The tomatoes themselves could potentially become the source of increased nutritional or medicinal benefit.



Eugenio Butelli and Yang Zhang

Professor Cathie Martin said:

“Our study provides a general tool for producing valuable phenylpropanoid compounds on an industrial scale in plants, and potentially production of other products derived from aromatic amino acids. Our work will be of interest to different research areas including fundamental research on plants, plant/microbe engineering, medicinal plant natural products, as well as diet and health research.”

Dr. Yang Zhang, said: “Our research provides a fantastic platform to produce valuable medicinal compounds in tomatoes. Medicinal plants with high value are often difficult to grow and manage, and need very long cultivation times to produce the desired compounds. Target compounds could be purified directly from tomato juice. We believe our design idea could also be applied to other compounds such as terpenoids and alkaloids, which are the major groups of medicinal compounds from plants.”

This research was strategically funded by the BBSRC, the EU ATHENA collaborative project, the Major State Basic Research Development Program (973 Program) of China, the John Innes Foundation, and the DBT-CREST Fellowship.

Project leader Cathie Martin reveals her dream: plant scientists can contribute innovative ways of looking and understanding the benefits of food in our diets

A role for plant scientists in promoting health



Cathie Martin

After almost 10 years of European collaborative activities on anthocyanins and health, ATHENA project leader Cathie Martin sums up the major achievements and future perspectives in the field of plant studies for human health.

Cathie, what are your thoughts at the end of the ATHENA study?

In one way, it's really sad because this is a group of friends who have been working together for almost 10 years and this is, for sure, an added value to the whole project. Our strength has been putting in contact from different disciplines, and allowing them to work together on national and international activities. We started our partnership with the FLORA study and the promising results we obtained convinced us to take another step forward; this is how ATHENA was conceived. Now, after 5 years of collaboration, we definitely reinforced our belief that dietary anthocyanins are really good for health. Our major task now is understanding how can we actually change the way people eat, and encourage them towards healthier diets.

Do you think we are ready to tell people anthocyanins are good for health and encourage them to add these compounds to their diet?

I think we should. We haven't found anything negative

about anthocyanins but only positive effects for health. It is true that most of our studies are still in animals, but actually I cannot see any reason to discourage people from consuming larger amounts of foods rich in anthocyanins.

It's time for clinicians to start looking at these data and thinking about prevention which is just as important as therapy. Intervention with food as combination therapy in chronic diseases can do a lot to ameliorate the outcome.

What are the other steps ahead?

We definitely need to try to apply the knowledge we generated over the last 10 years of research.

We need to find ways we can encourage consumption of anthocyanin-rich foods in everybody's diet. In general, our commitment is to deliver an evidence-based message for health. This should be the task of people who can really make the difference in the health field. I am talking about clinicians, but also food companies.

Do you think the ATHENA research team shall get back together again?

It would be lovely to meet up again. But I also think it's time for a new generation of people to lead new projects. What would be the best for me, as a fundamental scientist, would be that plant science was recognized as being able to contribute very innovative ways of looking and understanding the benefits of food in our diets. I'd love to see one day medical people finally saying "yes, plant scientists can help me in evaluating the good things in the foods we eat". This is very important, I think.

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