

Athena NEWS

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AnThocyanin and polyphenol
bioactives for Health Enhancement
through Nutritional Advancement

Interview with the coordinator of the Project Cathie Martin during the kick-off meeting in Milan

Flavonoids and health: the questions Athena will try to give an answer

The scientific team of Athena bears a considerable responsibility, since it inherits a scientific legacy from the Flora project which produced extremely interesting results regarding the beneficial effects of flavonoid supplementation of diets. What new findings do you expect from this second project?

Of course I am confident that we fulfil this scientific responsibility because everyone in the group is so enthusiastic. The results that came from the Flora project actually surprised people, particularly those who were skeptical at the beginning. Just to cite an example, the discovery of the relationship between polyphenols and omega-3 polyunsaturated fatty acid metabolism is just fantastic and it is absolutely new.

What was the impact of Flora on public health?

We've really contributed a lot not only to improving people's diet but also to understanding the mechanisms by which these phytonutrient compounds (such as flavonoids) work. And I also think there is a real interest from governments and public health bodies who are looking for new strategies to improve the quality of life of citizens and to prevent diseases. The Athena project can contribute to this task in a very unique way.

So what do you expect at the end of the Athena project?

I think we will be in a much better position to address questions like "can anthocyanins be toxic?" We can't actually answer this question, currently. I mean, I don't believe they are toxic, but we will put the issue to the test. Moreover, we can do comparative analyses between different flavonoids for their health benefits for the very first time. So we could say that resveratrol is better than anthocyanins or vice versa. Nobody else has ever been able to do that before. We can say whether these things work or do not work in humans. Most of the data up to now have come from experiments on animals but with Athena we are ready to verify the effects of phytonutrients in humans.

Are GMO an effective way to achieve healthy targets?

I believe genetically modified organisms could actually provide a healthier option for people who can't get healthy food on a regular basis due to lack of availability or cost. In such cases, GMO can allow consumers to get good sources of healthy compounds (phytonutrients) in ketchup or even on pizza. Bad food might also be made a little bit better. I think that one contribution from GMO could be to add something good to what people eat every day. In my opinion it is almost impossible to change people's dietary habits so we are called to set out new strategies to improve the type of foods they already eat each day.

The ATHENA research team during the first meeting in Acireale, Sicily, hosted by Italian partners



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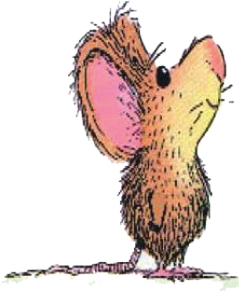
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Of mice and men

Of flavonoids and calories

Marco Giorgio talks about similarities between caloric restriction and flavonoids



The first experiments date back to 1934, when it was noted how laboratory rats fed with very low-calories diet had longer lives and better health conditions during their

ageing. The concept of caloric restriction was born. In the past decade, many researches, still limited to animal models for now, tried to explore the biological mechanisms taking place when one gets very, very hungry. And something new appeared on the horizon of longer lives and healthy ageing: the role that flavonoids can play in obtaining the same effects of caloric restriction.

This is one of the fields in which Athena Project is particularly involved, so we talked of caloric restriction, flavonoids and aging with Marco Giorgio, scientist at European Institute of Oncology, one of the members of Athena.

Eating very few calories, without reducing vitamins and other micronutrients intake, is not such an easy task for humans. Can flavonoids offer us the same opportunity?

What we have now, from experiments conducted by us and by other groups all over the world, is phenomenological evidence in this field. In details, we see how a flavonoid-rich diet is capable of "mimicking" caloric restriction, not only regarding macroscopic effects, but also at molecular level. In mice fed with anthocyanins, for example, we see an increased activity of enzymes involved in burning fat, while adipogenesis is reduced. The result is that balance between fat building and fat burning is shifted toward the last.

Apart being quite slim, what else do you see happening to these mice? Are they healthier?

Yes, and again we have a mimicking. In lab mice, we know that caloric restriction can delay onset of tumors and reduce ischemic damage to heart. Well, flavonoids-rich diet has the same effect, and the amplitude of it is similar. So we have a phenotype evidence. It could be enough to start tri-

als in humans. But of course we want to investigate deeper. We want to find mechanisms behind this. It means finding common metabolic and biochemical pathways, common signals that both caloric restriction and flavonoids send to cells. It is not so easy. Usually cancer cell lines are used for this kind of researches. But cancer cells present mutations just in those pathway we want to study. So we will use stem cells instead. More difficult to handle, but more useful for us.

So an animal gets a longer and healthier life. Is it possible that its offspring will get benefits too?

We can find pathways, as I told before. But it is more complex than this. Receptors are activated on cell membranes, signals are sent to the cellular nucleus.

Then something happens: expression of certain genes will be modulated. So we enter in the field of epigenetics. Chromatin [the complex of proteins that surround DNA regulating gene expression – editor's note] can be modulated by caloric restriction as well as flavonoids. And this could lead to inheritance".

Is it a mere coincidence that plants produce such useful compounds for animals?

I like to think of it as a co-evolution. Animals eat fruits, and doing so they disseminate seeds on a territory. Plants, therefore, obtain a great advantage if animals are healthier and live longer, so they can walk long distance, carrying seeds in their stomach and gradually disseminating them on a wider area. Plants need healthy animals, and flavonoids can be just their way to help.

We talked a lot of mice. What about humans and flavonoids?

We already know that eating lots of fruits and vegetables is quite good for our health. And we already can get flavonoids from the five-serving-a-day rule. At the moment, this is the best advice we can give.



The challenge of enriched foods to get low-cost healthy habits

High anthocyanin-content food is too expensive for the majority of people. Scientists from the University of Milan are trying to take a healthy shortcut

Eating healthy food is not just a matter of goodwill. In most cases, eating behaviors are somehow linked to reasons other than personal choices. One of those is an economic issue. Many studies have highlighted so far that healthy dietary habits are strongly related to greater economic availability showing how poorer people end up with having unhealthy diets because of the need to save money.

It is unquestionable that healthy food is quite expensive. Buying fresh fruits and vegetables or fish for example has become a luxury choice for families all over the world. Moreover, the lack of time to prepare proper food is strongly influencing dietary habits shifting toward westernized eating models with sneaky consequences for health. The increasing epidemic of obesity registered at every latitude of the globe is a striking

evidence of this trend.

That is why science has decided to put a brake on this by thinking about new ways to help people getting safer food. Enhancing traditional foods with healthy compounds

could represent a good solution.

“Having a daily amount of berries is definitely a good habit for everyone- says **Chiara Tonelli** from the University of Milan, who is responsible of model-foods within the Athena project - They’re rich in anthocyanins which have been proven to have healthy effects on human health. The point is that not everybody can afford such an expense. Berries are extremely expensive. Eating 100 grams a day might drain families’ budgets. The only solution is to increase the availability of sources of bioactive compounds. We are talking about new foods as the ones we are experimenting at

our university within the Athena project”.

“We created a new corn line by matching two genotypes and obtaining the black corn type which is rich in anthocyanins - **Katia Petroni** from the University of Milan argues - We’ve also started working on the tropical line, which has higher anthocyanin content since it has bigger seeds and thicker tissues.

The greatest news is that we created a special flour from purple corn which is 8-times richer in anthocyanins compared to the flour obtained

from seeds. This is because we extracted the flour from the cob – the hard part of the ear - which has high content of Anthocyanins. Moreover the biscuits obtained with this cob flour taste good even though they’re not ready to be commercialized yet. These biscuits will be used in the human trial of the Athena project which aims at seeing whether large consumption of anthocyanins is able to reduce the skin damage caused by radiotherapy in women affected by breast-cancer”.

“Our biscuits – Tonelli continues – have also a longer shelf-life than fresh berries so people can easily stock them and always have ready-to-eat healthy food”.

« Not everybody can afford such an expense. Berries are extremely expensive.

Eating 100 grams a day might drain families’ budgets. »



Spin-offs, SMEs and the role of genetics in Athena: interview with Daniele Cusi

Doing research the fast way



Within the Athena project Kos Genetic will conduct an epidemiological study to determine interaction between anthocyanin consumption, genetic structure and HDL levels in humans. Genotyp-

ing and genomic data analysis are important to pave the way towards a personalized Medicine and personal nutrition. We discussed these topics with Daniele Cusi, director of the Filarete Genomic and Bioinformatics Platform, a spin-off from the University of Milan which gave birth to Kos Genetic.

Considering your spin-off experience, do you think it is possible to draw some general indications on this kind of initiatives, about their role in research?

Our spin-off was born mainly out of necessity. At that time we had a European project underway and we needed to update our equipments quickly, otherwise we risked to not conclude the project. So we tried this adventure, and it worked very well.

This happened three years ago. What is the situation now? And what lessons have been learned?

We are going on quite well in some aspects. What we miss are techno-transfer capitals. In Italy we do not see many business angels supporting you and providing funds for technology transfer, something that should be the main role of a spin-off. We lack this kind of infrastructure. But the idea is really good, and we strongly believe in it.

Is the lack of techno-transfer capital driving the European Union to push SMEs, and spin-off like yours, presence into EU projects?

EU knows very well that academic world often is not a good money manager. SMEs, on the contrary, are "hungry", they must use money very wisely and very efficiently. So they are a good way to speed research processes. At the same time, EU projects aims to save SMEs in this difficult economic situation.

In your experience, what are the strong points of an Italian spin-off?

Well, it must be said that we do not manage to properly sell research products. Nevertheless, we are very efficient in putting things together, and make them work. Let me give you an example: we have strong relationship with Singapore.

They say they have young Chinese people working with them, skilled and competent. But they say "we lack gray hair". They mean experience, efficiency, good organization. Our spin-off, like others in Italy, represents gray hair so often needed. We are quite good in putting things together and make them work. We are fast and focused, and this is something not so often present in Academia.

What about your role in Athena?

Our WP is very linear, we can say that is somehow isolated from the rest of the partners' tasks. But I think that it will find a real synthesis ahead in the future, when more knowledge will be developed by partners. I choose to have this huge panel of genetic knowledge not to analyze them entirely right away, rather to have a databank from which mining what we will need. Of course, we hope to have suggestions from other partners' experiments. Another thing we offer to Athena is flexibility. We can stay updated with new technologies, we can move fast. Next year we could discover to need something new, well, we can deliver it.

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