



Article: Anna Prats-Puig, et al.
Soluble CRT3: A Newly Identified Protein Released by Adipose Tissue That Is Associated with Childhood Obesity.
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Guest: Dr. Anna Prats-Puig is a researcher in pediatric endocrinology at the Girona Institute for Biomedical Research in Spain

Bob Barrett:

This is a podcast from *Clinical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

Childhood obesity is a common disorder that predisposes individuals to increased risk for developing obesity and cardiovascular disease in adult life. Effective prevention and treatment of obesity-related disorders requires a better understanding of the key elements and early markers for body weight regulation and obesity. Recent studies have shown that the CREB regulated transcription co-activator 3 or CRT3 may be a promising new marker for obesity as it is thought to promote obesity through disruption of catecholamine signaling in adipocytes.

The March 2016 issue of *Clinical Chemistry* published a paper that examined if CRT3 is secreted by adipose tissue, if it can be measured in the circulation, and if so, are serum concentrations related to metabolic risk markers in children. Dr. Anna Prats-Puig is the senior author of that paper and she joins us in this podcast. She is a researcher in pediatric endocrinology at the Institute for Biomedical Research in Girona, Spain. Doctor, why do you measure circulating CRT3 in children?

Dr. Anna Prats-Puig: Because I'm from a pediatric research group and we are interested in studying cardiovascular disease markers in children. We also believe that in order to prevent the development of obesity and some obesity-related disorders, we need to understand better and we need to study obesity and also to study new markers just to prevent it. In accordance with that, we were reading some papers and I was interested in one paper published in *Nature* six years ago where some colleagues suggested that CRT3 could be a promising new marker for obesity.

They also reported that CRT3 knockdown mice fed with a high-fat diet were protected from obesity, insulin resistance, and hepatic steatosis. We did some more research just to know if humans there were some studies that were reporting some results about CRT3. We realized that there were only two studies showing some polymorphism in

CRT3 gene, showing that this gene weren't related to cholesterol level and the risk of being overweight. But none of them studied CRT3 in the circulation.

So, knowing that there are many, many proteins that are involved in intracellular and extracellular compartments, and that they have different functions in each compartments, we've decided to try to assess CRT3 in circulation. And in fact, we succeeded in it.

Bob Barrett: And what were the main findings of your study?

Dr. Anna Prats-Puig: First of all, we started assessing the secretion of CRT3 by the adipose tissue. So we collected some adipose tissue explants from healthy children in our hospital and we just cultured them. We found that CRT3 could be measured in the condition and media of the adipose tissue explants indicating that maybe CRT3 could be secreted by the adipose tissue elsewhere in our circulation. We also compared visceral and subcutaneous adipose tissue because we collected both of them and we cultured both. And we detected that visceral rather than subcutaneous adipose tissue secreted more CRT3 in the culture medium of our adipose tissue explants.

We decided that maybe it would be possible to detect also CRT3 in blood samples. We tried to quantify CRT3 in serum samples from our children by both, ELISA and Western blot. And we found that CRT3 could be measured also in circulation. So in fact, CRT3 is in blood, but we don't know what it is doing there. My guess that CRT3 is secreted partly by the adipose tissue.

To know if CRT3 could play some role in the circulation, we tried to find some correlations between CRT3 and some metabolic or anthropometric parameters that we also assess in children. What we obtained was that higher concentrations of CRT3 in blood were related to a higher BMI, higher waist circumference, higher systolic blood pressure, and diminished concentrations of high molecular weight adiponectin in our cross-section of the study.

To study further those associations, we wanted to study those associations in our longitudinal study because we also collect from children after three years from the baseline of the study.

In this goal, with the results that we have was that basal concentrations of CRT3, higher basal concentrations of CRT3 in fact was related to changes in BMI, weight, and also high molecular weight adiponectin and HDL cholesterol. We suggest that CRT3 at seven years of age can predict abdominal fat deposition and an increase in high molecular

weight adiponectin level. We also speculate that maybe CRT3 and high molecular weight adiponectin could be reciprocally regulated.

A possible mechanistic explanation that we give to our result is that visceral adipose tissue in children may secrete more CRT3 into the circulation which can diminish the activity of beta adrenergic receptor receptors leading to an accumulation of lipids in our adipocytes, and this can predispose to obesity.

Bob Barrett: So, doctor, should clinicians and scientists pay attention to circulating CRT3 concentrations in children or in adults or in both?

Dr. Anna Prats-Puig: Yes, that's a good question. I would like to think or believe that, yes. But it's too soon to say that because we are the first group showing that CRT3 can be found in circulation. Before deciding if clinicians or scientists have to pay attention to these CRT3 concentrations in blood, more studies are needed to clarify if CRT3 could be used as a biomarker or not, depending on the role that it may have in the development of obesity. Maybe it's just an elimination product and what we are seeing is just an increased secretion by the adipocytes. But we know that during obesity, we have more adipocytes and maybe, it's just a reflection of this BMI increase, what we are seeing. More studies are needed to see what we are seeing is a role that it's playing in the CRT3 in the circulation or not.

Bob Barrett: So finally, doctor, let's look ahead. What's next in this field of research?

Dr. Anna Prats-Puig: Yes. As I have said, there is too much work to do yet. And we have found CRT3 in the circulation so it's there in children at least. This has to be replicated in other population just to know if CRT3 is playing a role, in fact is doing something, in some kind of cell or it's just there because it's an elimination product of adipocytes. In fact, we believe that CRT3 can be internalized into some target cells for example the same adipocytes or hepatocytes or muscle cells. And there, CRT3 could play a role predisposing to obesity or insulin resistance or some obesity-related diseases.

For that reason, we believe that more studies using animal models, for example, mice without adipose cells, as well as more studies in obese or insulin-resistant subjects or other subjects would be interesting just to disclose whether CRT3 could have an active role in the development of obesity or if it's just an elimination product.

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We believe that it could have a role in the development of obesity and we believe that if some other group can just study the mechanistic role of CRT3, maybe they can demonstrate that CRT3 is having an active role in the development of obesity.

Bob Barrett:

That was Dr. Anna Prats-Puig. She is a researcher in pediatric endocrinology at the Girona Institute for Biomedical Research in Spain and she has been our guest in this podcast from *Clinical Chemistry* on new markers for childhood obesity. Her paper on that topic appeared in the March 2016 issue of *Clinical Chemistry*.

I'm Bob Barrett, thanks for listening!