

## CLAUDIN-16

**Catherine Chaussain** – I have always had an absolute passion for biology, it has always been my thing. When I was little, I used to catch all the mice that I came across and all the bugs that went by. I would cut them all up and put them under the microscope, I think that I had a microscope when I was seven years old! And then I used to boil everything up and make skeletons so yes, this is something I have always adored. And subsequently I studied to be a dentist while at the same time studying science and then when I was thirty-seven I said to myself, I'm missing something, and I left for a year's post-doc in the United States at Chicago. When I got back, I took on the leadership of this laboratory and I managed greatly to progress this theme, the link between the skeleton, teeth and rare diseases. Because when you have rare diseases that attack the skeleton, teeth are bound to be impacted and unsightly and therefore to show the correlation between the skeleton and teeth and rare diseases like osteogenesis imperfecta, brittle bone disease or genetic rickets. Now this has really been the heart of my work. And then one day, six or seven years ago, an American researcher discovered at the same time as a group of European researchers a new gene, we always knew that there would be one... a link between the kidney and the mineralisation of teeth. This is what in particular gives the wonderful tissue that covers the tooth called enamel, that lets you smile and bite because it is a very hard tissue. They discovered mutations, many mutations of this gene that gave pathologies where there was a problem at the level of tooth enamel, perhaps a complete absence of tooth enamel that is problematic, and calcifications of the renal parenchyma.

OK, so I was consulting at the hospital one Wednesday like any other on all my little rare diseases residents and in comes a charming young girl from the Congo who says to me: "Please Madam, I am very distressed, I have no enamel on my teeth...". I have a look at her teeth and yes, she has what we call an amelogenesis imperfecta, that is to say a total absence of enamel. OK... and I ask: "Do you have only the one problem or do you have other problems in other parts of your body?" And she replies: "Well yes, I have a kidney problem, my kidney mineralises all the time, it gets calcified..." . Aha... now I was very proud of myself and I found all my little interns and I told them: "Voilà! A patient who probably has a mutation on this new gene that has just been announced that is called FAM..." That is to say FAM, not like the French for 'female' but F, A, M... So I tell them: "That is probably my first patient with FAM because it is quite rare so it is the first that I have seen with this problem of enamel and kidney disfunction..." And she interjects: "Well I am followed by a nephrologist at Robert Debré so why don't you call her?" So I call the nephrologist at Robert Debré who tells me: "Oh no, not at all, it's not the FAM gene, It's another gene

that is called Claudin!” Now between the FAM genes and the Claudins... These are proteins whose function is to bind, called binding junctions, that do indeed bind cells to one another. And in fact a mutation on this Claudin was known to give renal calcification. So I ask her: “But do you have many patients?” “Oh”, she replies, “twenty or so patients in France.” My question is: “And have you looked at their teeth yet?” and her response: “No, never!”. OK...So I see the other patients, I manage to examine five or six and all do indeed have anomalies in their tooth enamel and I tell myself this really must be significant! And it has never been reported! So I decided to look in the literature and see if anyone has made a mouse. And I find a nephrologist who has made a mouse whose Claudin-16 gene is absent! I look on the internet, find his telephone number at la Charité in Berlin and he tells me: “Yes, I have the mouse but I never thought to look at the teeth! But if you like, I can send you some and in three days you will have the mice...”. Well I say: That’s fantastic!” So I get three mouse couples, very sweet, who arrive all wriggling and I see that they have teeth that are completely broken...All my team got to work on this and we found the link, finally, between the teeth and the kidney and we showed that this Claudin 16-gene was expressed in both the kidneys and also in the teeth. This has been one of my most thrilling discoveries.

**4 min 19 s**

Translated by Adrian Travis