# A STORY INSIDE A STORY

**Aleksander Edelman** – When I'm working in the lab, I'm a bit weird. Sometimes my mind brings up images that were impressed on me; they make it a kind of duty or obligation to do my best. Every scientist tries to do his best, of course, but I have this thing from History that keeps telling me that those who died in extermination camps were surely better than I am, that they never had a chance to advance science, so I have to do my utmost.

I came to France a few years after '68. It was sort of epic. I had five dollars in my pocket really… and I enrolled in the University. I didn't speak French. I don't know how I passed the exams, likely due to lenient professors who had just come back from demonstrations. I've been working on cystic fibrosis for thirty years by coincidence. I was in New York at the Columbia Medical School, in 1988. Everyone was trying to understand why there is a lung defect in cystic fibrosis patients.

In France, two hundred children are born with this disease every year. And until about ten years ago, the disease was fatal; even today children still die of cystic fibrosis, but now things are improving. Cystic fibrosis is a genetic disease, transmitted by parents. The gene causing the disease encodes for a CFTR protein whose function is that of the chloride channel, meaning that it conveys chloride ions. It was soon understood that this protein was a limiting factor for transport of water and ions through the epithelia, specifically in the lungs. This–is the mechanism that fluidifies the lung surface, clearing it of bacteria. For children with cystic fibrosis, the mucus is thick, bacteria come in and that's it... In the past, a lung transplant was the only treatment. Today we know that a mutation in the CFTR gene, the defected gene, occurs in about 70% of the patients. The protein encoded by this gene (the function of genes is always to encode proteins), happens to be badly folded and doesn't work properly.It is therefore soon degraded and ceases to function. I witnessed the discovery of the gene, I also witnessed identification of more than 2,000 mutations, and, very soon, we understood that everyone had to be treated, more than 2,000 mutations! And in our lab, with Iwona and Isabelle - the researchers with whom I work - we showed that we could predict the response of a sick child to a therapy and adapt it. This was the first concept: personalized therapy. Then I witnessed the discovery that defects occur at all levels of protein production, so defects are to be corrected at each level. It's another concept, multitherapy.

At the beginning of the 21st century we, in our laboratory, proposed that other proteins besides the mutated CFTR protein are important for a proper functioning of the lung epithelium, and that these proteins interact somehow with the mutated CFTR protein. We used the general approach called proteomics to find them. We found a very important protein called Keratin 8. When we

interrupt the interaction between the mutated protein and this one, the folding of the mutated protein improves, and it becomes functional! Of course, studies continue in order to improve treatments. Cystic fibrosis isn't cured, but it can be treated.

It was probably in 2005 or 2006 that I obtained a European project to work on cystic fibrosis using proteomics approaches. I decided that the first meeting would take place in Poland: some partners were Polish, others were English, Portuguese... We met in Warsaw, in a pre-war luxury hotel, neighbouring the Warsaw ghetto - I mean, where it had been in 1943. Well, we worked for two days, and I managed to put an early end to the meeting. So I invited all the participants to a tour in the Warsaw ghetto. As we walked around, we kept on conversations about proteins and gene defects. Then we slowly reached the Ghetto resistance memorials. There, I started to tell the story; colleagues listened. We walked to Samuel Zygielbojm's memorial - he had committed suicide during the war in London; he had attempted to draw the world's attention to what was going on in Poland for the Jews, and had failed, so he killed himself. A bit further on, I brought my crowd to the site of the bunker where Anielewicz and other resistance fighters had committed suicide. So my listeners were getting really moved and stopped talking science.

And finally, I led them to the hospital entrance, next to the Umschlagplatz,, the station from which trains left to Treblinka. And I told them, "You see, it's a hospital. Here too, during the war, doctors took care of children, and not just children. But they were somewhat like you, they practiced research as well - research on the sickness of famine. It was done very carefully, scientifically, just like today's research, only with the means that were available to them. Nearly all those doctors died of hunger, of famine, or were sent to Treblinka." A few survived, not many, and just after the war they published their work, in Polish. And even today, it's the only book that describes the symptoms of famine. It's a reference book.

One day, the doctors heard that the hospital would be evacuated the following morning, and all the children sent to Treblinka, the extermination camp. Having heard that, the doctors acted that night: they took the morphine that they had kept for themselves, in order to commit suicide if they were to be sent to Treblinka, and gave it to the sleeping children, who never woke up. So the doctors protected the children from dying in a gas chamber. At the time, parents kissed the hands of those doctors, who had saved the children from a terrible death. But today, those doctors would be judged harshly for such behaviour. But morals in wartime differ from morals in peacetime… Any questions?

**08 min 26 s**