

# Claude KLEE

## A Free French Scientist

By Jacques HAIECH

I met Claude Klee for the first time in 1978. She came to Montpellier when I was finishing my PhD and trying to purify Calmodulin from Brain. At this time, brain was considered as the organ with the higher titer of Calmodulin. But brain is a fatty tissue and we were obtaining miserable amount of the protein. Claude was already a star in the Calmodulin field and she suggested to us to use testis instead of brain. And the next morning, we went to the slaughterhouse to get several kg of ram testis. It was a success. Suddenly, we were getting grams of Calmodulin. Sometimes in Science, it is better to use testis than brain to be successful...



Claude obtain a MD in the 50s at the faculty of Medicine, La Timone, in Marseille (France) and then went to US in 1960 to specialize in neurosciences but instead, she spent 1 year to study tRNA. Doing melting curves, she starts to discover the wonderful world of biophysics.

She came back to Europe for one year in the laboratory of Pr M. Staehelin in Basel where she met her husband, Werner Klee, and be acquainted with the purification of proteins. Then, she came back to US in the laboratory of Lou Sokoloff (NIH) in 1962 where she was starting to study protein-protein interaction during four years.

Then, she joined the laboratory of Maxine Singer in the Institute for Arthritis where she studied the polynucleotide phosphorylase during two years. She quitted the team of Maxine to study a new enzyme (Histine ammonialyase) in the laboratory of Herb Tabor during four years.

We are in the first half of the 70s and Richard Nixon launched a national cancer program in order to eradicate this disease in the next 10 years. The National Cancer Institute is created and Maxine Singer with Bob Golberger moved to this new NIH institute. Maxine asked Claude to join her and she accepted only if free to work on her own subject. She wanted to study protein-protein interaction and the new emerging couple (Calmodulin-phosphodiesterase) seduced her. Nobody at this time realized the importance of this two proteins in the cross-talk between the calcium signal and the cAMP signaling pathway.

She took times to polish the techniques and the protocol that were needed to purify Calmodulin in order to build a Calmodulin affinity column allowing the purification of Phosphodiesterase. Using brain extract, Claude realized rapidly that Calmodulin was interacting with much more proteins than only Phosphodiesterase. Then, she played with different parameters in order to specifically bind and to elute Phosphodiesterase. Unfortunately, PDE was always a minor band whereas the main contaminant of the preparation was composed of two proteins in equal amount of 59 and 15 Kdaltons. The two proteins were the two subunits of a unique protein. The small subunit was

identified as a member of the calcium binding family with EF-hand motifs. As the protein was present in brain and was a calcium binding protein, the whole protein was named Calcineurin.

Calcineurin was in search of a function for almost three years and it was in the laboratory of Phil Cohen that Claude found that Calcineurin is a Calmodulin-Phosphatase in 1981.

For almost ten years Claude was able to decipher the role and the structure of Calcineurin without being annoyed by any competitors. Shortly later, Calcineurin was identified as the target of the immunosuppressor drug, FK506 and therefore, of the previous immunosuppressor drug, cyclosporine I. Then, Calcineurin became a protein star and nothing was the same in the field of immunology.

I was a post-doc in the laboratory of Claude at the real start of the Calcineurin story. I felt that it was fool to work on a contaminant. As a mathematician ,I was right from a logical point of view but I was wrong from a biological point of view.

Although Calcineurin is not everywhere (and at least not yet in the nucleus), the protein is a crucial node in several important regulatory pathways and Claude will stay always the one who discovers this biological central hub, regulating the cell balance between life and death.

Claude has always be supportive of the European Calcium Binding meetings and of the principles of the European calcium Society that guide our actions :

- Disseminating scientific information's to young scientists in an affordable meeting,
- Considering scientific information's as a public treasure and not as a mean to promote individualities,
- Promoting Excellence and Pleasure in Science as a mean to increase solidarity and exemplarity among generations of scientists,
- Bashing scientific misconducts as Science is also an art and not only an element of an economical open market.

Although pessimistic about the destiny of our World, she insides believes in the youth and most of the post-doc that she trains have profoundly matured after experiencing a Claude KLEE's Training program.

**Our European Calcium Society is proud to have Claude Klee as an honorarium member.**