It all started when I sat down with Yasutomi Nishizuka at the garden party given for the participants of the fourth International Conference on Cyclic Nucleotides and Protein Phosphorylation held in Brussels on July 25, 1980. Actually, I should say that the whole story started after completion of my PhD thesis. When Nishizuka described to me the properties of an enzyme (which he referred to as protein kinase C) that had recently been discovered in his group at Kobe University, it was more thrilling to me than about visiting Zen stone gardens in Kyoto than about the potential discovery of the receptor for tumor promoters.

I arrived in Kobe on August 1. We rapidly confirmed that phorbol esters such as thrombin were able to aggregate platelets and trigger serotonin release. Then we showed that, in contrast to thrombin, phorbol esters did not affect phosphoinositide metabolism. However, we provided evidence that phorbol esters enhanced phosphorylation of the 40 Kd protein, a major substrate of protein kinase C in these cells. Finally, we set up the experiment with purified protein kinase C on August 24. The prediction turned out to be right: phorbol esters substituted for diacylglycerol and in doing so mimicked physiological signals. I just had time before packing to write a draft manuscript and draw conclusions in a group seminar. When the plane took off from Osaka on September 1, I had not had much time for touring, but I had the feeling that I had completed my assignment.

The success of this project was made possible because I found in the Department of Biochemistry at Kobe Medical School a group of well-trained staff members headed by a restless, deeply dedicated scientist, who was able, due to his royal sense of hospitality, to create beneficial interactions among the participants of this study.

Back in France I applied for grants and working space. One year later I was ready to resume this research. The paper came out in June 1982. Interestingly, three reports in 1983 from American laboratories extended our contribution, attesting to an amazing adjustment to a new concept.

The paper has been cited frequently because phorbol ester C is a key enzyme in a signaling pathway common to neurotransmitters, hormones, mitogens, and many biological effectors. Phorbol esters are used as tools for investigating the transduction of these extracellular signals.


