The Discovery of Saporin

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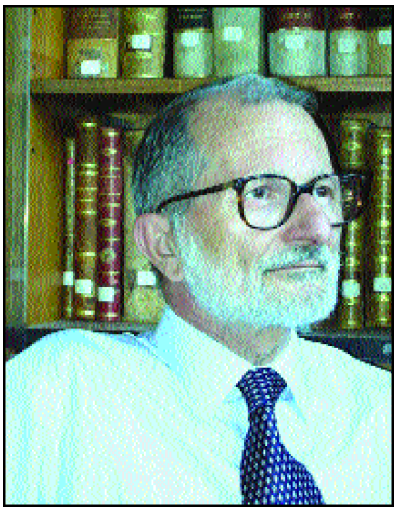

Professor Fiorenzo Stirpe
The discoverer of Saporin

toxins of the same kind existed in the plant kingdom. This began our search for other toxins and prepared extracts from all toxic plants we could get, mostly from tropical countries. Instead of testing these extracts for toxicity to animals or cells, for the sake of simplicity and rapidity, we assayed their capacity of inhibiting protein synthesis in a cell-free system. Indeed, in the course of some years we succeeded in identifying new toxins, namely modeccin, viscumin and volkensin. However, we soon found that some extracts inhibited cell-free protein synthesis, but were only some thousand-fold less toxic than ricin to cells or animals. At first we did not know how to interpret these "disturbing" results, until it was found that PAP, the pokeweed antiviral protein, inhibited protein synthesis with the same mechanism as ricin (2). It was then easy to ascertain that our active extracts contained proteins similar to PAP, which later on we called "ribosome-inactivating proteins" (RIPs). We decided to search for other RIPs, and since PAP had antiviral activity, we examined extracts from plants known to contain antiviral properties. Among these was *Dianthus caryophyllus* (carnation), from which we purified two RIPs, dianthin 30 and dianthin 32 (3).

Another approach was to explore plants in the same families as those plants with antiviral properties. Among these there was the Caryophyllaceae family, to which the carnation belongs. One of the plants investigated was *Saponaria officinalis* (soapwort), which was growing in the garden outside our department in Bologna, exactly under the window of my office. Much to our astonishment, the seeds of *Saponaria* turned out to contain several very active RIPs we called saporin (4). Saporin-S6 was used in the construction of immunotoxins (5) and subsequently by Drs. Douglas Lappi and Ronald Wiley for the preparation of a range of conjugates that are excellent experimental tools for the study of the nervous system.

So, after having struggled to search for seeds from all over the world, more or less by chance we isolated one of the most widely used RIPs from something that was literally under our feet.

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