

Chevreul Medal Lecture:

Exploring Fat Digestion: From Molecular Aspects to Clinical Studies

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The multidisciplinary approach adopted by our laboratory involves know-how in two scientific fields which have been associated with the city of Marseille ever since the 1950s: the biochemistry of lipolytic enzymes and the physiology of the pancreas. Studies on these lines were first launched by Professor Pierre Desnuelle, an earlier winner of the Chevreul Medal, and Professor Henri Sarles, who won international recognition in gastroenterology. Today, the biochemists from our laboratory are still working side by side with physicians on gastrointestinal lipolysis, ranging from the lipase molecular aspects to clinical trials on healthy human subjects and patients. These concerted efforts are quite unique and they have led to the development of some useful tools for the quantitative investigation lipolytic processes in vivo. It was thus possible to determine in terms of mass the secretion of the main human digestive lipases –gastric and pancreatic lipases- during test meals and their respective contribution to the lipolysis of dietary triglycerides. Later, these tools were used in clinical studies on lipase inhibitors for reducing obesity (Orlistat®) and on novel lipases for enzyme replacement therapy in patients with pancreatic insufficiency. At the molecular level, the aim of our basic research projects is to elucidate the processes underlying the main stages in enzymatic lipolysis: the adsorption of lipases onto lipid/water interfaces, conformational changes of the lipase to adapt to its new environment and substrate hydrolysis. The specificity of lipases can depend on either of these stages. Understanding the functional specificities of lipases and finding ways of adapting them as required is a major challenge, since lipases have many potential biotechnological applications (detergents, structured fats and oils, fine chemistry, etc.) as well as the medical applications previously mentioned. In the latter respect, our laboratoire is particularly interested in pancreatic and gastric lipases, but has also been actively involved in the characterization of novel pancreatic lipases (pancreatic lipase-related proteins 1 and 2), the role of which only starts to be elucidated. All these developments will be reviewed in the Chevreul Medal lecture.