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Editorial

Saliva and fetal life

Jörgen Ekström

Emeritus Professor, Department of Pharmacology, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden

"Unity is strength:
the Cagliari-Rome axis"

Keywords

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Corresponding author

Jörgen Ekström, MD, PhD, BSc, Emeritus Professor, Department of Pharmacology, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden; email: jorgen.ekstrom@pharm.gu.se.

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In humans, Textbooks usually highlight the important roles of saliva in chewing and swallowing, contribution of digestive enzymes and taste, protection and healing of the oral cavity, and speech. However, in the present review by Cabras and colleagues (published in this issue) [1], using non-invasive collection of saliva, the reader is brought into a new unexplored territory for salivary research in humans: the composition of saliva of preterm newborns and the potential functions of saliva and salivary glands during fetal development – is there, for instance, a trophic role for saliva to play?

The study on the salivary proteome during the last months of gestation and during growth took its start in the early 2000s under the leadership of professor Massimo Castagnola and professor Irene Messana at the University of Cagliari (Italy), to the initial credit of professor Alessandro Riva, the eminent expert on the morphology of salivary glands. The studies benefitted from the expertise of professor Gavino Faa, yet another eminent researcher of the Cagliari University, who joined forces in order to apply immunohistochemical techniques on fetal tissues obtained at autopsy. In collaboration with colleagues of the Institute of Neonatology at the University of Cagliari and the Institutes of Biochemistry, Neonatology and Otorhinolaryngology at the Università Cattolica del Sacro Cuore of the Policlinico Agostino Gemelli in Rome (Italy), the original observations on the salivary proteome of preterm infants served as an important impetus for numerous studies of the research team aimed at understanding the properties of the proteins characterized in the salivary proteome and their functions during development and, for comparisons, into adulthood. Salivary glands are thought to be fully developed at a gestation age of 28 weeks [2], so the early time (25-26 weeks) chosen by the authors represents a late stage of gland development; at this time, acidic proline-rich proteins are already secreted as shown by the present authors, but at low concentrations, reaching adult values at about the age of 1 year. Other salivary proteins were found to display different patterns, a high concentration at this early time of observation but hardly detected in full-term newborns or obtaining high concentrations first at the age of puberty. Consequently, and importantly, due to the great variations in the concentrations of specific proteins over time, the authors warn for conclusions drawn from proteomic studies if not relating the findings to the age of the individuals being studied. Of great interest is the authors' attempt to associate specific proteins with specific functions during fetal development or at later ages. And here, the authors draw particular attention to thymosin β_4: a protein present in cytoplasmic granules of both minor and major glands and in the secreted saliva during fetal growth but not observed in infants. The authors do not only associate thymosin β_4 with the growth of the oral cavity but also, due to their finding of its widespread distribution in the body, with the fetal growth of a number of tissues and, further, they introduce a tentative role for the protein in tumor growth. In a complementary animal study, they show thymosin β_4 administration to the maternal mouse to accelerate both the skeletal growth and the growth of a number of visceral organs of the fetus, opening the fascinating idea that the protein may be used during late pregnancy to treat human fetuses at risk. Saliva has been suggested to serve as a biomarker in order to diagnose various diseases and to monitor their progression as well as the effect of treatment; the field for its potential use is continuously expanding [3, 4]. The present authors have also pursued this line of research [5], for instance, demonstrating in the present review a proteomic protein profile of saliva signalling prodromes of autism spectrum disorders at an early stage. Of particular interest in this review is the comparative result obtained by studying the DNA of ancient hominids, which shows how the structure of some proteins rich in proline evolved in *Homo sapiens* compared to Neanderthals, a phenomenon probably linked to the different feeding habits of modern man, compared to the ancient. The present team has received international recognition, exemplified by awards from the International Association of Dental Research.

The use of saliva in clinical practice, with its non-invasive technique, makes great promise of a wide area of applications for diagnostic and prognostic purposes, a major prerequisite for progress and success being, however, solid knowledge in the biochemistry of saliva. A steady flow of well-written, outstanding salivary proteomic studies has emerged over the years from the Cagliari-Rome team, and continues to do so. This review summarizes a gigantic analytic work over more than two decades using top-modern equipment and illustrates how today the coordination of various research groups on a common topic can generate significant progress aimed at characterizing the molecular events underlying human life.

Though the focus of the present review has been on the exocrine role of salivary glands, one may wonder, eventually, whether the salivary glands also have an endocrine role to play, for instance

releasing growth factors to the blood stream during development – an issue evidently waiting for its response in the future.

Declaration of interest

The Author declares that there is no conflict of interest.

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