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Parotid Gland Comparative Microscopic Anatomy

Histología Comparada de la Glándula Parótida

Ignacio Roa[1,2] & Mariano del Sol[3]

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SUMMARY: The frequent use of animal models in biomedical research means that the anatomy or histology of the animals is constantly analyzed so the results obtained can be extrapolated to human tissues; therefore, knowledge of the structures studied is truly important. This study compares the human parotid gland to that of three animal species from a histological point of view. Five parotid gland samples from each animal species were used: Sprague Dawley rats (*Rattus norvegicus*), C57BL/6 mice (*Mus musculus*) and male rabbits (*Oryctolagus cuniculus*). The samples were stained using H/E, Masson trichrome and van Gieson's techniques. The anatomical relations of the parotid glands in the three species were the facial nerve, master muscle and mandibular ramus among other anatomical elements. Histologically, the duct system in the three species is comprised of intercalated, striated, excretory ducts and main excretory ducts. Human, rodent and rabbit parotid glands are made of purely serous adenomeres. The intercalated and striated ducts are prominent. The human parotid gland is well characterized by intralobular adipose tissue, as is observed in rabbit, whereas the adipocytes are not prominent in the parotid gland in rats and mice. The tissue of the rat parotid gland contained a large number of serous acini that included a large area of gland tissue and few ducts, as observed in the rabbit and human. The glands studied present considerable morphological similarities with the human one that make them reliable candidates as experimental models of parotid tissue.

KEY WORDS: Parotid gland; Compared histology.

INTRODUCTION

Rodents, lagomorphs and humans have three pairs of major salivary glands and numerous minor salivary glands distributed throughout the oral cavity (Hyman & Wake, 1992; Amano *et al*., 2012; Treuting & Dintzis, 2012). Their main role is the production and secretion of saliva, this being an essential component required in maintaining an ecological balance in the oral cavity (Vucicevic-Boras *et al*., 2001).

Saliva also aids in digestion and swallowing, lubrication and moistening of the mucosa, remineralization, anti-bacterial, antimycotic, antiviral activity, tissue repair, and activity related to the sense of taste (Dawes *et al*., 2015), with these functions being similar in rodents and humans.

The human parotid gland (PG) is developed from an ectodermal proliferation of the stomodeum during the sixth week of prenatal development (Moore & Persaud, 2002). It is the salivary gland of greatest volume, located behind and below the external acoustic meatus, partially covering the mandibular ramus and the masseter muscle, and it is closely related to the facial nerve that runs through it. It has a main excretory duct, the (Stenon or Stensen) parotid duct, which leaves the anterior border of the PG, passes in front of the masseter muscle, penetrates the buccinator muscle, and finally opens into the oral cavity at the level of the second upper molar (Standring, 2015).

In rodents, the PG is behind and below the ear, bordering the submandibular gland caudally (Jonjic, 2001). On the other hand in the rabbit, the PG has a location in the retro-mandibular and perimandibular region, also presenting a thin preauricular extension (Hakim *et al*., 2002). In all the species the PG is intimately related to structures such as the mandibular ramus, masseter muscle, facial nerve, external acoustic meatus, and other anatomical structures.

Increased research in the biomedical area and the need to use in vivo models makes animal experimentation ever more necessary (Nilsson *et al*., 2012). This being the case, knowledge of the histological organization of the anatomical structures is essential to harmonize results with the structure in humans (Amano *et al*., 2012).

[1] Unidad de Morfología, Departamento de Ciencias Básicas Biomédicas, Facultad de Ciencias de la Salud, Universidad de Talca, Talca, Chile.
[2] Programa Doctorado en Ciencias Morfológicas, Facultad de Medicina, Universidad de La Frontera. Temuco, Chile.
[3] Centro de Excelencia en Estudios Morfológicos y Quirúrgicos (CEMyQ), Universidad de La Frontera, Temuco, Chile.
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The aim of this study was to analyze and compare the histology of the parotid glands of three species of mammals with the human one.

MATERIAL AND METHOD

Samples of the parotid gland from adult male specimens were used: Sprague Dawley rats (*Rattus norvegicus*) (n=5), mice (*Mus musculus*) (n=5) and rabbits (*Oryctolagus cuniculus*) (n=5), which were euthanized with an overdose of ketamine/xylazine. The tissue samples were fixed in 10 % buffered formalin for 72 h and embedded in paraplast. Then, 5 µm sections were obtained, which were dyed using the H & E, van Gieson's and Masson's trichrome techniques, and photographed under an ICC50W Leica® DM750 50W microscope (Leica, Nussloch, Germany). Finally, the histological description was made of the samples from the three species.

RESULTS AND DISCUSSION

Parotid gland microscopic anatomy

Parotid gland stroma. In all the species studied, the salivary glands are composed of clusters of epithelial tissue immersed in connective tissue, presenting two portions: the terminal portion (adenomere) (area of saliva production) and ducts (Fig. 1).

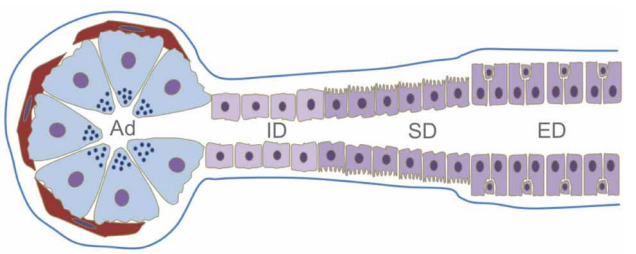

Fig. 1. Scheme representing organization of a salivary gland. Ad: Adenomerus, ID: intercalated duct, SD: striated duct, ED: excretory duct.

The human PG is covered by a thick layer of irregular dense connective tissue that acts like a capsule, from which a series of trabecules emerge that subdivide it into lobes and lobules. Blood vessels enter and leave through this connective tissue, as does the ducts (Fig. 2C). Those of the human, rat and mouse have characteristics similar to those present in the rabbit PG, which contains a large amount of white adipose tissue at the level of the capsule and trabecule, with capillaries and arterioles also being present among the unilocular adipose cells, tissue found in the human, although in a smaller proportion (Fig. 2A-B).

The connective tissue in humans, rats and mice is introduced and surrounds each glandular structure, being represented mainly by limited collagenous tissue available in irregular bundles at the level of the intercalated and striated ducts and more abundant collagenous tissue at the excretory level, accompanied by fibroblasts among the fibers (Fig. 3A-D). In the case of the rabbit PG, this presents little connective tissue around each structure, replaced by white adipose tissue that infiltrates both the stroma and parenchyma (Fig. 2B).

Parotid gland parenchyma

Parotid gland terminal portion. The terminal portion (adenomere) present in the PG has an acinus (spherical) shape, and is comprised of pure serous cells with a small central lumen. The pyramidal epithelial cells have a truncated apical vertex and a nucleus surrounded by condensed chromatin, shifted basally, in addition to a large number of secretory granules full of zymogens (Fig. 3E-H). In sections stained with H/E, the cytoplasm is densely basophil at basal level and acidophil at apical level, and also presents a large number of mitochondria, rough endoplasmic reticulum (RER) and Golgi apparatus, organelles typical of secretory cells, characteristicspresent in human, rat, mouse and rabbit, an observation similar to what was reported by Amano *et al.* (2012) and Al-Saffar & Simawy (2014), and different from what was described by Flavia *et al.* (2017), who indicated that rabbit adenomeres had a seromucinous appearance. Around the adenomere it is possible to distinguish stellate myoepithelial cells, as well as around the intercalated ducts (Leal *et al.*, 2003; Amano *et al.*, 2012).

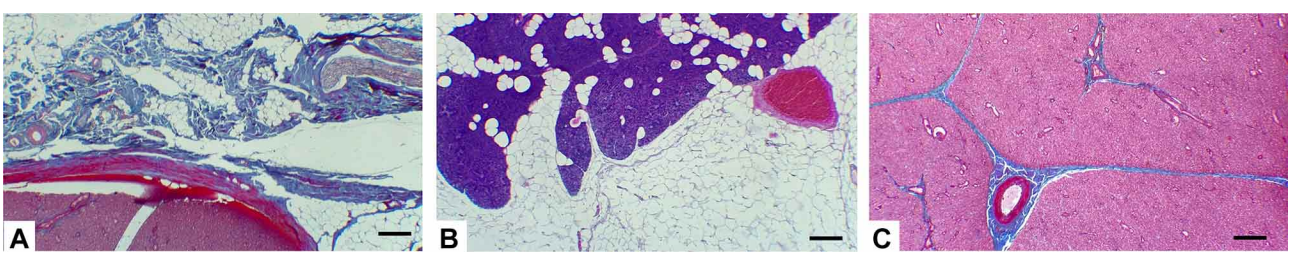

Fig. 2. Presence of white adipose tissue in conective capsule and trabecules (A-B). Division of parenchima in lobes and lobules (C) barr 200 µm. H & E, and Masson's trichrome techniques.

Duct System of the Parotid Gland. Like the human salivary glands (Amano, 2011; Brüel *et al*., 2015), the duct system in rodents and rabbits is made up of intercalated ducts (ID), striated ducts (SD), excretory ducts (ED) and main excretory ducts, with these last ones leading to the main excretory duct (MED) (Fig. 1).

Intercalated duct (ID). In all species, the ID is located between the adenomere and the SD, receiving the primary saliva directly from the adenomere. It is characterized as being a smaller duct made up of low cuboidal epithelial cells, presenting a round central nucleus (Fig. 3I-L), being partially covered by stellate myoepithelial cells. Connective tissue and blood vessels surround the ID.

The ID serves a passive function in the transport of the primary saliva. Some authors maintain that these ducts represent a population of undifferentiated cells that can become differentiated in cells of the adenomere or SD.

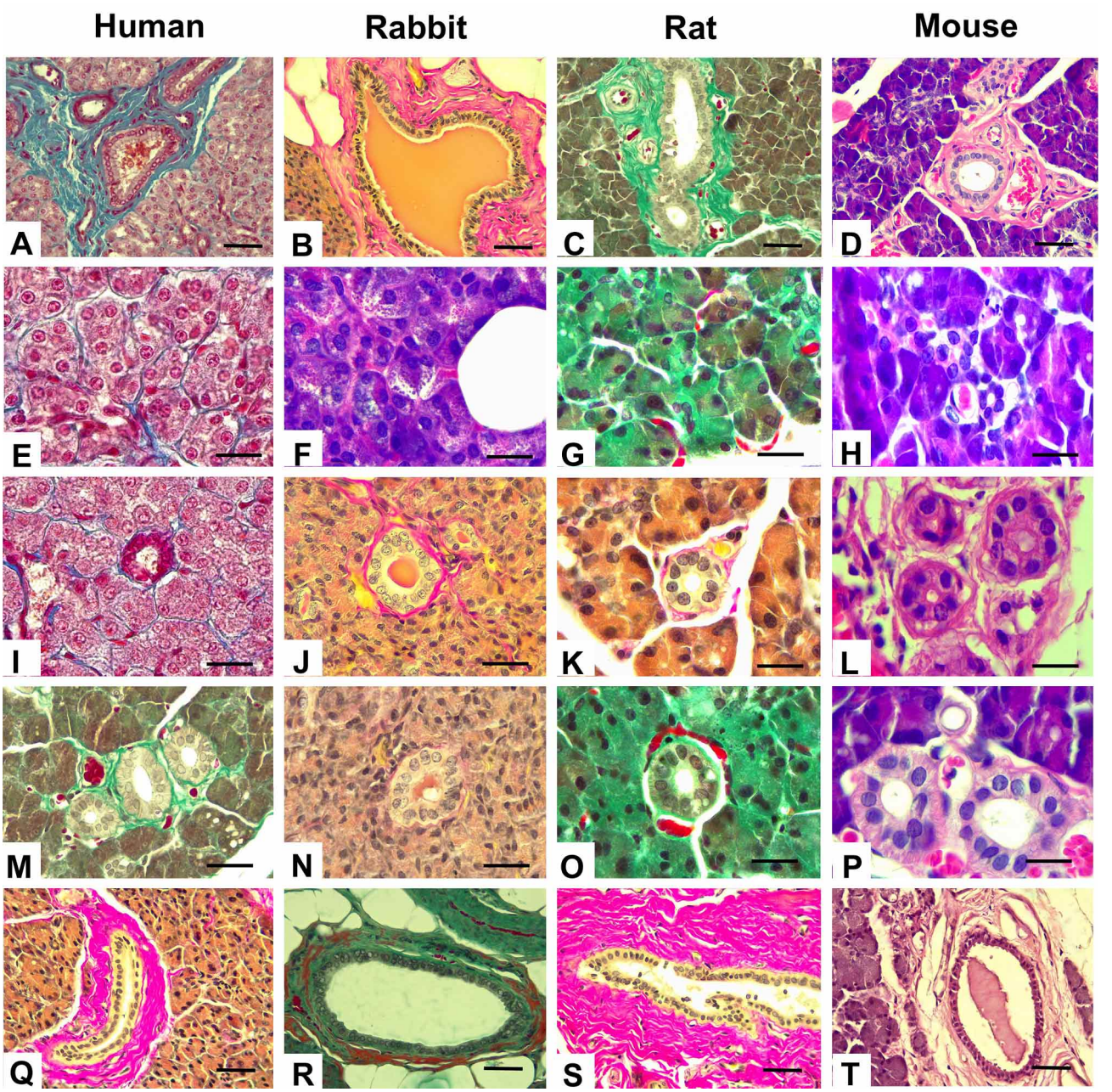

Fig. 3. Histological structures of parotid gland of human, rabbit, rat and mouse. Blood vessels and ducts in conective trabecules (A-D), barr 100 µm. Adenomerus (E-H), barr 50 µm. Intercalated duct (I-L), barr 50 µm. Striated duct (M-P), barr 50 µm. Excretoy duct (Q-T), barr 100 µm. H & E, van Gieson's and Masson's trichrome techniques.

Striated duct (SD). The SD is a specialized portion of the duct system, the function of which is to transport electrolytes bidirectionally between the ductal lumina and the extracellular spaces for secretion and resorption. The cuboidal or columnar epithelial cells have a markedly acidophil cytoplasm and centrally located spherical nuclei when stained with H/E (Fig. 3M-P). Masson's trichrome and Van Gieson's stains reveal the abundance of blood vessels around the duct (Fig. 3 M,N,O).

The cells that make up the ducts reveal a characteristic basal striation, which is observable with the H/E, Masson's trichrome and Van Gieson's stains, striations composed of multiple folds accompanied by long mitochondria. Other ultrastructural characteristics are poorly developed RER and Golgi apparatus accompanied by some elements of an apically located smooth endoplasmic reticulum (Gómez de Ferraris & Campos Muñoz, 2009).

Excretory duct/main excretory duct (ED/MED): These are characterized as being covered by a simple columnar epithelium with eosinophil cytoplasm cells with few basal striations (Fig. 3 Q-T) that gradually disappear and which is gradually transformed into pseudostratified columnar epithelium. The MED that leads to the oral cavity is ultimately covered by non-keratinized stratified squamous epithelium the same as the oral mucosa.

Without a doubt, the morphology analyzed in the parotid gland of both lagomorphs and rodents displays considerable similarities to the morphology present in the human being, from both the anatomical and histological points of view. Therefore, the parotid glands of these animal models are good candidates for the experimental analysis of pathologies or the effects of drugs or radiation (Cakmak Karaer *et al*., 2016; Mattioli *et al*., 2016). They are good animal models not only due to their morphological similarities with humans, but also because these animals are easy to maintain and reproduce (Hau & Van Hoosier, 2003; Nilsson *et al*.).

CONCLUSIONS

The salivary glands of rodents and lagomorphs, animals used as experimental models, show great histological similarity to human glands, which makes them excellent candidates as experimental models. The knowledge in this case is vital to better interpret the results.

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RESUMEN: El frecuente uso de modelo animal en investigación biomédica, hace que constantemente sea analizada la anatomía o histología de dichos animales, donde los resultados obtenidos deben ser extrapolables a tejidos humanos, por lo cual el conocimiento de las estructuras estudiadas, es realmente importante. El presente trabajo compara a la glándula parótida humana con las de tres especies desde un punto de vista histológico. Se utilizaron muestras de glándula parótida de ratas Sprague Dawley (*Rattus norvegicus*) (n=5), ratones (*Mus musculus*) cepa C57BL/6 (n=5) y conejos (*Oryctolagus cuniculus*) (n=5) machos, las cuales fueron teñidas con técnicas de H/E, Tricrómico de Masson y van Gieson. Las glándulas parótidas analizadas se relacionaron anatómicamente en todas las especies con elementos tales como nervio facial, músculo masetero, rama mandibular entre otros. Con respecto a la histología, el sistema de conductos de roedores así como de conejo se compone de conductos intercalados (ID), estriado (SD), excretor (ED) y conductos excretores principales. Las glándulas parótidas humanas, de roedores y conejos están compuestas de adenómeros serosos puros. La ID y SD son prominentes. La glándula parótida humana está bien caracterizada por tejido adiposo intralobular, al igual a lo encontrado en el conejo, mientras que los adipocitos no son prominentes en la glándula parótida en ratas y ratones. El tejido de la glándula parótida de la rata se observaron gran cantidad de acinos serosos que comprenden una gran área del tejido de la glándula y unos pocos conductos, al igual que el conejo y humano. Las glándulas estudiadas presentan semejanzas morfológicas considerables con la humana que las hacen candidatas confiables al momento de su elección como modelos experimentales del tejido parotídeo.

PALABRAS CLAVE: Glándula parótida; Histología comparada.

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Corresponding author:
Dr. Ignacio Roa
Unidad de Morfología
Departamento de Ciencias Básicas Biomédicas
Facultad de Ciencias de la Salud
Universidad de Talca
Lircay Av. s / n
Talca
CHILE

E-mail: iroa@utalca.cl

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