

第 36 回生理研コンファレンス

第 36 回生理研コンファレンスは、日本学術振興会平成 18 年国際学術集会助成事業として、第 3 回ニールス・ステンセン記念国際唾液腺シンポジウムおよび生理研研究会と合同で 2006 年 10 月 20 日から 23 日の会期で自然科学研究機構 岡崎コンファレンスセンターにて開催された。

本会は対象を唾液腺に限定し、形態学、生理学、生化学、薬理学、病理学、細胞生理学の研究者達の成果のすりあわせを同じテーブルで行い、新しい概念を模索し臨床応用へ連結する芽を育むことを目的とした。14 ヶ国から 50 名、国内から 70 名の唾液腺分野の第一線研究者が集い講演 40 題、ポスター 60 題が発表された。

- A. 唾液による化学診断と分泌蛋白のプロテオミクス：唾液を臨床データとして取扱うための重要な合意として、唾液分泌速度と唾液中の基質濃度の関係図を作成し、この相関から評価すべきことが議論された。分泌蛋白/ペプチドの分析がこの5年間のマスマスプロトコプの技術革新で本格的に稼働し始めた。分泌蛋白は細胞内分泌顆粒内で貯蔵され、細胞から分泌され、導管を通る間にも修飾をうけ、さらに口腔内でも修飾を受けることが議論され、数多くのフラグメントについても将来の研究課題として残された。
- B. 唾液機能を付与するための遺伝子治療：喉頭がん、咽頭がんなどの放射線治療により唾液腺の腺房など分泌末の機能が失われる。腺房の機能を導管に肩代わりさせ、水分分泌機能を加えるプロジェクトが本年アメリカ公衆衛生院 (NIH) で開始された。基礎研究が具体的な臨床応用に発展した希有の例であり、聴衆を大きく勇気づけた。
- C. 環境変化に応じた唾液分泌調節の神経機構：従来あまり問題にされていなかった唾液腺からの求心性信号の存在が確定され、これがどのように中枢に作用し、唾液分泌を統御するか次に探索することとなった。唾液減少症に用いられるピロカルピンが脳室周囲系を刺激し「口渇」を誘導することが示された。このため、体液量調節の観点から、本薬の唾液分泌作用との関連が複雑になることが指摘され、本薬を含む研究の問題点が明らかになった。
- D. 唾液腺構造分化と機能発現：唾液腺が発達段階で枝をはり、管腔を形成する。唾液腺での幹細胞を探索し、これを唾液腺機能不全患者に自己移植し機能を回復させてゆくことは唾液腺分野の組織工学者の目標である。本会では幹細胞の探索の成果、接着分子の細胞内骨格の制御が討議された。
- E. 分泌顆粒の機能形態：分泌顆粒が均一ではなく下部構造をもつことは既に報告されてきたが、今回、グリコーゲンの沈着が幼少期の唾液腺分泌顆粒の傍らに発見され、顆粒の成熟との関係が注目された。また顆粒のアクアポリン 6は陰イオン輸送を介し分泌顆粒内物質の濃縮を制御することが議論された。
- F. 経傍細胞輸送調節：細胞からの水分分泌と細胞の間を通過する傍細胞輸送による水分分泌について、アクアポリン 5を浸透圧受容体としてその信号により傍細胞経路が開閉する説が初めて国際学会で高く評価され、具体的な実験プランも直接研究者間で相談された。
- G. 分泌開始を誘導する細胞内信号系：Ca 信号系について12年前に岡崎で開催された唾液腺ワークショップからの研究史が総括され、細胞内 Ca ストアの実態として連結した小胞体のアイデアが提出、今後細胞内信号系の実態を微細形態学で観測する手法が話し合われた。

生理学研究所は2007年創立30周年を迎えるが、これまで岡崎市民には大きな支援を受けてきた。今回その恩返しと基礎研究を市民に理解していただくため、市民公開講座と市民公開演奏会を開催し、歴史的な学問の基盤と国際的な広がりを体感していただいた。会場の岡崎コンファレンスホールにシンポジウム参加者と岡崎市民、岡崎 3 研究所の職員、高校生ら約200名が参加し、講演とリュートの演奏を味わった。



20 October Friday

CITIZEN FORUM

Opening Lecture: Alessandro Riva (Cagliari) The work of Fabricius ab Aquapendente (Harvey's Teacher) in the light of the recently restored Tabulae Pictae: its influence in the development of modern anatomy in Europe and in Japan.

Lute Concert: Terrell Stone (Music Conservatory of Vicenza, Italy) Lute music from the court of Francis I and Padovan lute music.

21 October Saturday

SCIENCE SESSION

O. Opening of Science Session

Talk: Alessandro Riva (Cagliari) Stensen and early history of glands and exocrine secretion.

A. Diagnostics using saliva and Proteomics of Saliva

Talk: Masataka Murakami (Okazaki), Naoki Shinozuka (Sapporo) Clinical examination using saliva: Influence of fluid secretion on the concentration of substrate in saliva: How to overcome the problem for *in vivo* application.

Talk: Anders Bennick (Toronto) Extraoral functions of salivary proteins.

Talk: Josie A Beeley (Glasgow) Human salivary proteins- A fascinating complex of polymorphic and polyfunctional proteins.

Poster: Tiziana Cabras (Cagliari) A proteomic study of saliva from celiac patients.

Poster: Rosanna Inzitari (Rome) Salivary acidic proline-rich proteins in preterm newborns.

Poster: Tomoya Hayashi (Nantan, Kyoto) Oxidative modification of serum albumin via paracellular route of rat submandibular gland.

Poster: Marco Piludu (Cagliari) A preliminary study on salivary protein expression in diabetic patients.

Poster: Naoki Shinozuka (Sapporo) Clinical examination using saliva: an *in vivo* application to human adults.

Talk: Massimo Castagnola (Rome) How the technique works and how the researcher can take a profit from the MS strategies.

Talk: Francisco ML Amado (Aveiro) Salivary glands and saliva composition: a proteomic approach.

Talk: Irene Messana (Cagliari) Salivary peptides as potential substrates of type2 transglutaminase.

Talk: Massimo Castagnola (Rome) Pre-secretory Post-translational modifications common to different families of human salivary proteins.

Talk: Chenjuan Yao (Tokushima) Tissue kallikrein mK13 is a candidate of the processing enzyme for pro-IL-1b in the mouse submandibular gland.

Poster: Rui Vitorino (Aveiro) Protein content comparison of mouse submandibular and parotid salivary glands.

Poster: Chiara Fanali (Rome) Characterization of different proline-rich peptides from pig parotid glands.

Poster: Joanna Anton Monteiro, Massimo Castagnola (Rome) Tyrosine sulfation of Histatin 1. A post-translational modification specific of submandibular glands.

Poster: Hiroko Inoue (Kita-Kyushu) Different roles of salivary mucins in viscosity and spinnbarkeit of human saliva.

Poster: Takahiro Hayasaka, Mitsutoshi Setoh (Okazaki) MALDI based Mass Imaging revealed abnormal distribution of phospholipids in cancer.

B. Therapeutics by modulation of salivary gland

Video: Bruce Baum (Bethesda) Clinical applications of gene transfer to salivary glands.

Talk: Takayoshi Sakai (Osaka) Morphogenesis and cleft formation of salivary gland epithelia: Exploration of new functional regulators.

Poster: Naozumi Ishimaru (Tokushima) A novel role of RbAp48 for tissue-specific apoptosis in the salivary glands depending on estrogen deficiency.

Poster: Masatake Asano (Tokyo) Ionomycin inhibit the soluble protein transport between ER and Golgi.

Poster: Wei Muxin (Nanjing) Investigation on the influences of Chinese herbs on salivary secretion in rat submandibular gland.

Poster: Hideaki Kagami (Tokyo) Possible involvement of clusterin in the regeneration process of rat submandibular gland.

Poster: Wei Muxin (Nanjing) Effect of Dan Di Qiong Yu granule on salivary gland of Sjogren syndrome mice.

Poster: Tomoko Nashida (Niigata) Relation of proteoglycan to sorting amylase into secretory granules/vesicles.

Poster: Hiroshi Shimomura (Niigata) Activation of cAMP-dependent protein kinase by cGMP in the rat parotid acinar cells.

C. Neural control of salivary secretion in response to environmental change

Talk: Kiyotoshi Inenaga (Kokura) Pilocarpine induces salivary secretion and thirst in rats.

Talk: Ryuuji Matsuo (Okayama) Electrophysiological analysis of the afferent activity from the submandibular salivary gland in the rat.

Talk: Xuefei Li (Tokushima) Effects of autonomic denervation and administration of SNI-2011 on the expression of AQP5 in the rat salivary gland.

Talk: Jörgen Ekström (Göteborg) Neural- and hormonal-induced protein synthesis and mitotic activity and the dependence on NO-generation.

Poster: Kentaro Ono (Kita-Kyushu) Relationship of chewing-stimulated whole saliva flow rate and salivary gland size in humans.

Poster: Ken'ichi Ishizuka (Niigata) Cardiac-related activity in superior salivatory nucleus neurons in anaesthetized rats.

Talk: Yoshihiro Mitoh (Okayama) Electrophysiological study on the descending excitatory synaptic inputs to the superior salivatory nucleus in the rat.

Talk: David K Ann (Los Angeles) Functions, regulation and mechanisms of action of SUMOylation in salivary cells.

Poster: Akihito Fujii (Okayama) Electrophysiological study of the inhibitory inputs from the forebrain and brainstem to the superior salivatory nucleus in rats.

Poster: Miyuki Kobashi (Okayama) Role of the feeding center for submandibular salivary secretion during feeding behavior in the rat.

Poster: Nina Khosravani (Göteborg) The facial nerve and its influence on the parotid gland.

Poster: Hülay Çevik Aras (Göteborg) Melatonin-evoked protein secretion from the rat parotid gland *in vivo*.

Poster: Hajime Ishibashi (Matsudo) Induction of general anesthesia with propofol increases salivary flow.

Poster: Minoru Matsui (Tokyo) Salivary secretion by MR3-KO mice.

22 October Sunday

D. Structural differentiation and functional expression of salivary gland

Talk: Yohki Hieda (Osaka) Regulation of epithelial tube formation in developing mouse submandibular gland.

Talk: Matthew Hoffman (Bethesda) FGF10 regulates branching morphogenesis during salivary gland development.

Talk: Tetsuya Akamatsu (Tokushima) Involvement of a subtilisin-like proprotein convertase, PACE4, in branching morphogenesis and AQP5 expression in the rat embryonic submandibular gland.

Poster: Kenichiro Kikuchi (Tokyo) Freeze fracture studies of tight junctions in mouse salivary glands and cultured salivary cell lines.

Poster: Masanori Kashimata (Gifu) Shared or non-overlapping intracellular signaling pathways activated by EGFR or FGFR differentially regulate branching morphogenesis in fetal mouse submandibular glands.

Poster: Yuuichi Kadoya (Sagamihara) Cellular aspect of salivary gland branching morphogenesis.

Poster: Nunuk Purwanti (Tokushima) The expression of cellular markers of duct/acini and side population dynamics in the duct-ligated mouse submandibular gland.

Poster: Shinya Yamamoto, Satoshi Fukumoto (Fukuoka) Role of PDGF in salivary gland morphogenesis.

Poster: Wataru Masuda (Kita-Kyushu) The change of the subcellular localization of CD38 in the rat sublingual gland during saliva secretion.

D. Structural differentiation and functional expression of salivary gland

Talk: Arthur Hand (Farmington) Submandibular and sublingual glands in Nkx2-3 mutant mice.

Talk: Shoichi Iseki (Kanazawa) A novel mouse protein differentially regulated by androgens in the submandibular and lacrimal glands.

Talk: Kenji Mishima (Yokohama) Identification and therapeutic potential of salivary gland side population cells.

Poster: Osamu Amano (Sakado, Saitama) Heat shock protein 27kDa (Hsp27) regulates differentiation and regeneration of acinar cells of the rat submandibular gland.

Poster: Sachiko Matsuura (Shiojiri, Nagano) Temporary accumulation of glycogen in the epithelial cells during developmental differentiation of the mouse submandibular gland revealed by the high-pressure freezing/freeze substitution-TEM.

Poster: Miwako Matsuki (Matsudo) Effects of actin-related drugs on exocytosis in parotid acinar cells.

Poster: Sadamitsu Hashimoto (Chiba) Control of paracellular transport and its morphological evidence in perfused rat submandibular gland.

Poster: Atsuko Sato (Fukuoka) Localization of G proteins in the main excretory duct of the rat submandibular gland with special reference to the MED tuft cell and the taste bud type II cell.

E. Functional morphology of secretory granules

Talk: Bernard Tandler (Cleveland) Ultrastructure of the ovine parotid gland.

Talk: Alessandro Riva (Cagliari) A morphometric study by HRSEM of the secretory responses of human salivary glands stimulated *in vitro* by various secretagogues.

Talk: Hiroshi Sugiya, Miwako Matsuki (Matsudo) Expression and function of aquaporin-6 in the rat salivary glands.

Talk: David Giovannucci (Toledo, Ohio) Analysis of secretory dynamics in mouse parotid acinar cells reveals multiple pathways for secretory granule fusion.

Poster: Akane Imai (Niigata) Roles of Rab27 and its effectors in isoproterenol-induced amylase release from rat parotid acinar cells.

- Poster:** Matthew J Betzenhauser (Rochester) Subtype-specific regulation of inositol (1,4,5)- trisphosphate receptors by protein kinase A
- Poster:** Tomomi Nemoto (Okazaki) Exocytosis and fluid secretion in exocrine glands studied by two-photon microscopy.
- Poster:** Akiko Shitara (Ishikari-Tobetsu) Multi-photon imaging of cellular heterogeneity in the sensitivity of Ca^{2+} responses in rat parotid ducts.
- Poster:** Raffaella Isola (Cagliari) Morphological changes induced by histatins in *Candida albicans*: A microscopic and submicroscopic comparison.
- Poster:** Hideaki Tamaki (Sagamihara) Sequential appearance of Golgi proteins during *de novo* formation of the Golgi apparatus in parotid acinar cell.
- Poster:** Yosuke Tojyo (Ishikari-Tobetsu) Comparison of cluster formation of GFP-IP3 receptors in HSY, a human salivary cell line, and COS-7 cells.
- Poster:** Konosuke Kumakura (Tokyo) Possible Involvement of Myosin-ATPase in the spatio-temporal regulation of exocytosis in adrenal chromaffin cells.

F. Control for fluid/electrolyte transport via trans-/paracellular routes

- Talk:** James Melvin (Rochester) The ion and fluid secretion mechanism.
- Talk:** R James Turner (Bethesda) Structural and functional significance of the dimerization of the secretory Na-K-2Cl cotransporter (NKCC1).
- Talk:** Jun Yamazaki (Fukuoka) Localization and function of CLCA in rat submandibular glands.
- Poster:** Yusuke Imai (Otsu) Bond graph expression on an epithelial transport system.
- Poster:** Martin C Steward (Manchester) A modular approach to computational modelling of epithelial electrolyte transport.
- Poster:** Varga Gabor (Budapest) Bicarbonate secretion by cultured salivary gland cells
- Poster:** Chikara Hirono (Hiroshima) Regulation of Cl secretion by muscarinic cholinergic and adrenergic stimulation in acinar cells of rat salivary gland.
- Poster:** Yoshiro Sohma (Takatsuki) Voltage-dependent transient activity of Na^+/H^+ exchanger.

23 October Monday

F. Control for fluid/electrolyte transport via trans-/paracellular routes (continued)

- Talk:** A E Hill (Cambridge) A feedback control model of fluid transport in salivary gland.
- Talk:** Anil G Menon (Cincinnati) Evidence for interaction between transcellular and paracellular water transport pathways: signaling between Aquaporin-5 and the tight junction complex in mouse salivary glands.
- Talk:** Junko Yoshigaki (Matsudo) Change of claudin expression in primary cultured parotid acinar cells.
- Poster:** Christine Delporte (Brussels) Impaired aquaporin-5 distribution in salivary glands from a Sjögren's syndrome mouse model.
- Poster:** Mileva R Karabasil (Tokushima) Molecular and cellular analyses of mutant AQP5 which occurred naturally in Sprague-Dawley rats.
- Poster:** Retsu Mitsui (Matsudo) Regulation of intercellular junctions in polarized salivary cells.
- Poster:** Tetsuji Nakamoto (Rochester) The use of gene disruptions and isolated, perfused glands to examine mouse submandibular function.
- Poster:** Yoshiteru Seo (Mibu, Tochigi) Water permeability as measured by NMR in salivary gland cells.

G. Stimulus-Secretion Coupling for starting electrolyte transport

Talk: James W Putney Jr (Research Triangle Park) Calcium signaling mechanisms in salivary gland cells and other epithelial cells.

Talk: Akihiko Tanimura (Ishikari-Tobetsu) Monitoring IP₃ and Ca²⁺ dynamics in salivary and other cell lines.

Talk: David I Yule (Rochester) Intracellular calcium signaling: mechanistic insight from analysis of distinct signals in parotid and pancreas.

Talk: Jason Bruce (Manchester) Regulation of the plasma membrane Ca²⁺-ATPase in parotid acinar cells.

Poster: Philip Poronnik (St Lucia, Queensland) Muscarinic receptor mobilization of plasma membrane Ca²⁺-ATPase in epithelial cells: Role of the NHERF2 PDZ scaffold.

Poster: Jenny Ekberg (St Lucia, Queensland) Regulation of KCNQ2/3 by the ubiquitin ligase Nedd4-2.

Poster: Keitaro Satoh (Matsudo) Secretagogues stimulate phosphorylation of MARCKS in parotid acinar cell.

Talk: Shumuel Muallem (Dallas) Regulation of TRPC channels by STIM1.

Talk: Min Goo Lee (Seoul) Shank2 as a key regulator of epithelial transport in apical membrane.

Talk: David I Cook (Sydney) The regulation of the epithelial Na⁺ channels by UTP.

Talk: Anuwat Dinudom (Sydney) Signaling pathways regulating Na⁺ transport in salivary ducts.

Poster: Hideyo Yoshida (Takatsuki) Ca²⁺ influx induced by ionomycin under a high [K⁺] in rat submandibular acinar cells.

Poster: Il-Ha Lee (Sydney) Regulation of the epithelial sodium channel by caveolin.

Poster: Xibao Liu (Bethesda) The role of TRP channel in the salivary gland fluid secretion.