
1. BIOGRAPHICAL SKETCH

NAME: **Luisa Dalla Valle**

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POSITION TITLE: **Associate Professor, SSD BIO/06, Comparative Anatomy and Cytology (now BIOS-04/A)**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Padova, Italy	MSc	1983-1986	Biological sciences
University of Padova, Italy	Ph.D.	1988-1992	Comparative endocrinology
University of Padova, Italy	Post-doctoral Fellow	1993-1994	Comparative endocrinology
Istituto Zooprofilattico delle Venezie	Post-doctoral Fellow	1994-1995	Molecular biology
University of Padova, Italy	Post-doctoral Fellow	1996-2000	Endocrinology and developmental biology

A. Personal Statement

Since the beginning of my scientific career, my research has focused on steroid hormone synthesis and signalling, with particular attention on the extra-glandular steroidogenesis research field. Using a wide range of biochemical and molecular biology approaches, I investigated this process in animal models spanning nearly all vertebrate classes, reflecting my background as a comparative endocrinologist.

Findings from my PhD and postdoctoral work helped to challenge and redefine the classical view of steroid biology. Traditionally, steroid synthesis was believed to be restricted to endocrine glands, while peripheral tissues were considered sites of activation only. Our work contributed to demonstrate that steroidogenesis is widely distributed across tissues, where it is finely regulated in a developmental, tissues- and species-specific manner. We showed that steroidogenic enzymes expression is regulated in peripheral tissues using alternative promoters, a mechanism that enables tissue-specific regulation of local steroid biosynthesis outside classical endocrine glands. Moreover, we found that steroid synthesis is altered in pathological conditions, thus affecting hormone-responsive tissues, such as the endometrium, breast, thyroid and prostate. These discoveries contribute to the concept of “intracrinology”, first proposed in 1991 by Fernand Labrie (Laval University Medical Center, Quebec, Canada), in whose laboratory I trained during my PhD. Importantly, our results support the hypothesis that extra-glandular steroidogenesis anticipated the evolution of glandular steroidogenesis, suggesting that steroid hormone production would be a general cellular process that was later amplified in specialized endocrine glands to expand their regulatory influence.

After my initial research on steroids, I shifted my focus on steroid receptors, adopting zebrafish as a powerful vertebrate model. This work has revealed, and continues to reveal, how steroid hormones and their receptors, most notably the glucocorticoid (GC) receptor, regulate development and physiology.

To achieve this, I combined morphological, molecular and genetic approaches, including expression analyses, the generation of the transgenic biosensor line Tg(9×GCRC-HSV.UI23:EGFP)ia20, to dynamically trace GC activity in living embryos and adults, morpholino knockdowns experiments and CRISPR/Cas9 mediated generation of stable receptor-null mutants for androgen (*ar*^{-/-}), mineralocorticoid (*mr*^{-/-}) and GC (*gr*^{-/-}) receptors. Of note, while *GR*-null mice die perinatally due to lung maturation defects and *MR*-null mice die postnatally from renal salt-wasting and electrolyte imbalance, preventing studies beyond these stages, zebrafish *gr*^{-/-} and *mr*^{-/-} mutants are viable, allowing the investigation of Gr and Mr functions into adulthood. We also generated KO lines for enzymes involved in GCs synthesis (*cyp11c1*^{-/-}) or metabolism (*hsd11b2*^{-/-}). Both the transgenic line and the different mutant lines have been shared with several laboratories in Europe, the United States, and Israel to allow their use to improve our knowledge on many of the physiological processes in which these steroids are involved, and to elucidate the different roles played by Gr and Mr.

The works performed with these tools revealed, among other findings, that maternal GC receptor mRNAs are indispensable for proper development; that loss of GC signalling disrupts stress regulation, food-entrained circadian rhythms and reproduction; and that Gr and Mr interact to regulate gene transcription, providing new mechanistic insights.

In recent years, my expertise in zebrafish genetics and GC-Gr biology has opened new collaborative avenues in the field of neurodegeneration. I'm currently working with Prof. Nicoletta Plotegher (UNIPD) to investigate the mechanism by which β -glucosyl- β -sitosterol, a natural plant-derived compound absorbed through the diet, may contribute to the onset of a complex disorder called amyotrophic lateral sclerosis-parkinsonism dementia complex (ALS-PDC). Our central hypothesis is that this effect involves interaction with the GR. To address this, we are employing the zebrafish GC-related KO lines we generated, which offer a powerful tool to directly demonstrate receptor involvement.

My experience in CRISPR/Cas9-mediated zebrafish KO generation also led to collaborations in the autophagy research field in collaboration with Profs. Cecconi (UNICATT), Bonaldo, Carnevali (UNIVPM) and Sandri (UNIPD). Knockout lines for key autophagy genes (*ambra1a*, *ambra1b*, *epg5* and *mytho*) revealed the essential roles of this process in development, as gene disruption led to severe defects in organogenesis, skeletal muscle formation, heart morphogenesis and reproductive capabilities of the mutants. Importantly, Ambra1b proved to be critical for primordial germ cell survival, sex differentiation, and fertility, uncovering a previously unrecognized link between this protein and germ cells. Moreover, transplantation experiments of zebrafish morphant *ambra1a* or *ambra1b* cells into wild-type recipient embryos demonstrated the cell-autonomous capability of Ambra1-depleted cells to undergo hyperproliferation, confirming the role of this protein in the control of cell proliferation.

Additionally, *epg5* knockout line further established the relevance of autophagy genes in disease, recapitulating features of human Vici syndrome and offering a powerful platform for drug screening.

Finally, in collaboration with Prof. Nicoletta La Rocca (UNIPD), I recently applied the zebrafish model to study the anti-inflammatory and antioxidant properties of compounds of microbial origin, particularly exopolysaccharides and lipids extracted from the most abundant cyanobacteria in Euganean therapeutic muds. By validating their effects *in vivo*, we demonstrated their potential as natural bioactive molecules capable of modulating immune responses and oxidative stress, thus providing a scientific basis of the potential of mud treatments for recovery from chronic inflammatory diseases.

Beyond zebrafish, in the past my research has also contributed, together with Prof. Lorenzo Alibardi (UNIBO) and Prof. Leopold Eckhart (University of Vienna), to the understanding of the structure, diversity, and evolution of reptilian β -keratins (now better defined as keratin associated beta-proteins). This research highlights reptiles as key models for exploring how skin proteins evolved, how epidermal structures adapt to ecological pressures, and how regenerative success or failure is determined in different vertebrates.

During my post-doctoral activity in collaboration with the Istituto Zooprofilattico delle Venezie, I contributed to the development of sensitive and quantitative PCR-based assays for the detection of major fish pathogens, including betanodaviruses and *Photobacterium damsela* subsp. *piscicida*, improving diagnostic capacity in aquaculture.

B. Positions, Scientific Appointments, and Honors

2020	National scientific qualification for Full Professor - sector 05/B2 (Comparative anatomy and cytology) and sector 05/F1 (Applied biology) (from January 2020 to January 2029)
2014-Present	Associate Professor (05/B2, Comparative Anatomy and Cytology), UNIPD, Italy
2014	National scientific qualification for Full and Associate Professor - sector 05/B2 (Comparative anatomy and cytology) (from 24/02/14 to 24/02/20)
2001-2014	Assistant Professor (05/B2, Comparative Anatomy and Cytology), UNIPD, Italy
2000-2001	Technical assistant, Department of Biology, UNIPD, Italy
1998-1999	Research fellowship Department of Biology, UNIPD, Italy
1996-1997	Research fellowship, Ministero delle Politiche Agricole e Forestali, Department of Biology, UNIPD
1994-1995	Research fellowship project CEE AIRI CT92-0308, Department of Biology/Istituto Zooprofilattico delle Venezie

- 1993-1994 Research fellowship from “Sistema Lagunare Veneziano”, Department of Biology, UNIPD, Italy
- 1988-1992 Graduate Student, PhD in Comparative endocrinology, Department of Biology, UNIPD, Italy
- 1996 MSc Biological Sciences, Magna cum laude, UNIPD

Institutional responsibilities and organizing activities

- 2004-present Member of the Academic Board for the PhD school, initially in Comparative Endocrinology, later integrated into Regenerative Medicine, and, since 2013 integrated into the PhD School in Molecular Medicine.
- 2015-June 2025 Vice-President of the Aggregate Course of Study Board for Biology (Bsc), (MSc), and Marine Biology (MSc). Still a member of the Committee for Credit validation, the Committee on Teaching and the GAV (Group for Accreditation and Evaluation).
- 2015 Member of the local organizing committee of the 5th International Workshop on the Biology of Fish Gametes, 7-11 September 2015, Ancona (Italy).
- 2017, 2018, 2020 and 2023 President of the PhD Final Examination Committee for the PhD in Life and Environmental Sciences of the Doctorate in Life and Environmental Sciences, XXIX Cycle, UNIVPM; Member of the Committee for the PhD in Molecular genetics, biotechnologies and experimental medicine, XXX Cycle, UNIBS; Member of the Final Examination Committee for the PhD in Bioscience and Territory, XXXII Cycle, UNIMOL; Member of the Final Examination Committee for the PhD in Translational Specialist Medicine "G.B. Morgagni", XXXV Cycle, UNIPD, respectively.
- 2023: Member of the Final Examination Committee for the PhD Thesis of Halima M. “Ginsenosides as selective glucocorticoid drugs: agonists, antagonists, and prodrugs”, Institute of Biology, Leiden University.
- 2024 Member of the local organizing committee of the 31st Conference of the European Society for Comparative Endocrinologists, September 1-5, 2024, Ancona (Italy).

Commissions of trust

- 2012, 2015, 2016, 2020: Member of the selection committees for the evaluation of UNIPD post-doctoral positions and projects (PRID).
- 2017: Evaluator for the French National Agency (ANR).
- 2019: Evaluator for US-Israel Binational Science Foundation (BSF).
- 2021: Evaluator for AMF Telethon.

Scientific society membership

Member of the “European Society for Comparative Endocrinology”, “North American Society for Comparative Endocrinology”, “Gruppo embriologico italiano” and “International Society of Developmental Biology”.

Editorial activity

Reviewer for several international peer-reviewed journals, among them: Journal of Endocrinology, Molecular Psychiatry, Autophagy, Scientific reports, BMC Evolutionary Biology, Chemosphere, General and Comparative Endocrinology, Differentiation, Cells, Biomolecules, ETAP, Journal of Pediatric Endocrinology and Metabolism. Guest Editor and Section Board Member for IJMS.

Teaching/education (current courses)

Cellular Biology (72 hours, 8 ECTS), Bachelor’s Degree in Biotechnology; Developmental Biology (56 hours, 6 ECTS), Bachelor’s Degree in Biology.

C. Contributions to Science

1) Extra-glandular steroidogenesis. Key contributions of these studies include the demonstration of novel sites of steroid biosynthesis across multiple tissues of rat, trout, frog, bird and human; the identification of a paralog aromatase gene expressed in the brain of rainbow trout and the characterization of its regulation; the analysis of androgen production in the rat gastrointestinal tract and

the developmental regulation of P450c17 activity in the rat liver. We also revealed the potential for local estrogen synthesis and action in thyroid tissues and showed that their expression is increased in thyroid tumors, suggesting a potential role of these steroids in cancer development and progression. (21 papers in international journals, 15 as first or last name).

- Dalla Valle L, Couet J, Simard J, Labrie Y, Belvedere P, Simontacchi C, Labrie F, Colombo L. (1995). Occurrence of cytochrome P-450c17 and androgen biosynthesis in the oesophagus and gastrointestinal tract of the rat. *Mol. Cell. Endocrinol.*, 111(1):83-92.
- Vianello S, Waterman MR, Dalla Valle L, Colombo L. (1997). Developmentally regulated expression and activity of 17 α -hydroxylase/C-17,20 lyase cytochrome P450 (P450c17) in rat liver. *Endocrinology*, 138(8):3166-3174.
- Dalla Valle L, Ramina A, Vianello S, Fassina A, Belvedere P, Colombo L. (1998). Potential for estrogen synthesis and action in human normal and neoplastic thyroid tissues. *J. Clin. Endocrinol. Metab.*, 83(10):3702-3709.

2) Use of the zebrafish model and transgenic and mutant lines generation to uncover novel roles of steroid hormone receptors in development, stress adaptation, reproduction, and behavior, highlighting the role of maternal contributions. While encompassing all steroid hormone receptors, this research focuses primarily on glucocorticoids and their diverse roles in physiology. (12 papers in international journals, 10 as corresponding and last name)

- Pikulkaew S, Benato F, Celeghin A, Zucal C, Skobo T, Colombo L, Dalla Valle L. (2011). The knockdown of maternal glucocorticoid receptor mRNA alters embryo development in zebrafish. *Dev. Dyn.*, 240(4):874–889.
- Benato F, Colletti E, Skobo T, Moro E, Colombo L, Argenton F, Dalla Valle L. (2014). A living biosensor model to dynamically trace glucocorticoid transcriptional activity during development and adult life in zebrafish. *Mol. Cell. Endocrinol.*, 392(1-2), 60-72.
- Facchinello N, Skobo T, Meneghetti G, Colletti E, Dinarello A, Tiso N, Costa R, Gioacchini G, Carnevali O, Argenton F, Colombo L, Dalla Valle L. (2017). nr3c1 null mutant zebrafish are viable and reveal DNA-binding-independent activities of the glucocorticoid receptor. *Sci. Rep.*, 7, 4371.

3) In collaboration with Prof. Plotegher, we are currently using GC-related zebrafish mutant lines to investigate the possible interaction between the β -glucosyl- β -sitosterol and the glucocorticoid receptor. Our first paper is under review at “Journal of Biomedical Science”.

- Terrin F, Faggin S, Bizzotto E, Santinello D, Cerantola S, Borsato G, Fabris F, Scarso A, Licitra R, Guella G, Sales G, Cagnin S, Treu L, Bubacco L, Giron MC, Plotegher N, Dalla Valle L. β -glucosyl-sitosterol triggers intestinal inflammation in zebrafish and mouse models prior to neurodegeneration onset.

4) Generation of zebrafish KO lines to study autophagy. These studies revealed essential roles of Ambra1a and Ambra1b and autophagy-related genes in zebrafish organogenesis, muscle and germ cell development, sex differentiation, and reproduction, while establishing zebrafish models for human disease and providing evolutionary insights of the presence of Ambra1 outside vertebrate. (10 papers in international journals, 7 as corresponding and last name)

- Benato F, Skobo T, Gioacchini G, Moro I, Ciccocanti F, Piacentini M, Fimia GM, Carnevali O, Dalla Valle L. (2013). Ambra1 knockdown in zebrafish leads to incomplete development due to severe defects in organogenesis. *Autophagy*, 9(4), 476-495.
- Meneghetti G, Skobo T, Chrisam M, Facchinello N, Fontana CM, Bellesso S, Sabatelli P, Raggi F, Cecconi F, Bonaldo P, Dalla Valle L. (2019). The epg5 knockout zebrafish line: a model to study Vici syndrome. *Autophagy*, 15, 1438-1454.
- Fontana CM, Terrin F, Facchinello N, Meneghetti G, Dinarello A, Gambarotto L, Zuccarotto A, Caichiolo M, Brocca G, Verin R, Nazio F, Carnevali O, Cecconi F, Bonaldo P, Dalla Valle L. (2023). Zebrafish ambra1b knockout reveals a novel role for Ambra1 in primordial germ cells survival, sex differentiation and reproduction. *Biol Res.*, 56, 19.

5) Zebrafish organism model to study the potential of bioactive molecules. These studies investigated microbial polysaccharides extracted from Euganean thermal muds, revealing their consistent anti-

inflammatory and antioxidant activities in vivo using zebrafish models, and identifying the molecular pathways through which they modulate inflammation, thereby providing mechanistic insights into their therapeutic potential. (6 papers in international journals, 15 as last or co-last name).

- Zampieri RM, Adessi A, Caldara F, De Philippis R, Dalla Valle L, La Rocca N. (2022). In vivo anti-inflammatory and antioxidant effects of microbial polysaccharides extracted from Euganean therapeutic muds. *Int J Biol Macromol*, 209 (Pt B), 1710-1719.

5) Study of evolution, molecular diversity, and functional characterization of reptilian epidermal and defense proteins. These studies revealed the diversification of keratin-associated beta-proteins, the properties of beta-defensin-like peptides, and the molecular pathways underlying successful versus unsuccessful organ regeneration in amniotes. For the first time, we demonstrated that mammalian-type hair keratins are also present in reptiles, revealing an earlier, than previously supposed, evolutionary origin of corneous proteins and providing new insights into vertebrate integument evolution. (26 papers in international journals, 16 as first or last name)

- Dalla Valle L, Toffolo V, Belvedere P, Alibardi L. (2005). Isolation of a mRNA encoding a glycine-proline-rich b-keratin expressed in the regenerating epidermis of lizard. *Dev Dyn.*, 234(4):934-947.
- Eckhart L., Dalla Valle L, Jaeger K, Ballaun C, Szabo S, Nardi A, Buchberger M, Hermann M, Alibardi L, Tschachler E. (2008). Identification of reptilian genes encoding hair keratin-like proteins suggests a new scenario for the evolutionary origin of hair. *PNAS*, 105(47):18419-23.

6) Besides my contribution to the development of PCR-based assays to improve diagnostic capacity in aquaculture, the betanodavirus phylogenetic analyses we performed not only clarified their molecular evolution but also revealed recombination events occurring between different viral strains, highlighting a previously unrecognized mechanism that generates genetic diversity and enhances viral adaptability. (7 papers in international journals, 5 as first or last name)

- Toffolo V, Negrisolo E, Maltese C, Bovo G, Belvedere P, Colombo L, Dalla Valle L. (2007). Phylogeny of betanodaviruses and molecular evolution of their RNA polymerase and coat proteins. *Mol. Phylogenet. Evol.* 43(1), 298-308.

Publications in international peer-reviewed journals

At present, my scientific accomplishments include 111 papers published in international peer-reviewed journals. From Scopus, h-index is equal to 40 and the sum of citations is equal to 10,314 (25/09/2025).

Ongoing Research Support

Research agreement between Department of Biology, UNIPD and Centro Studi Termali Pietro d'Abano, 2025-2026, PI

FOOD for LIFE, PR Veneto FESR 2021-2027, CUP D19J24000670007 – 2024-2027, Participant.

Due to issues with the family name, the complete bibliography can be found only in Scopus (ID: 57577281500) or ORCID (<https://orcid.org/0000-0001-8097-6369>).

Padova, September 26, 2025

Luise Dalla Valle