BIOGRAPHICAL SKETCH

.

NAME: **Pierre RONCO**

eRA COMMONS USER NAME: RONCO

POSITION TITLE: **Emeritus Professor of Nephrology, Sorbonne Université, Académie nationale de médecine and Institut Universitaire de France**

EDUCATION/TRAINING: *Baccalauréat 1968, Medical Faculty Saint -Antoine, Université Pierre et Marie Curie (Paris 6)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Université Pierre & Marie Curie, now Sorbonne Université	MD	NA	07/1980	Medicine
Université Paris 7, Denis Diderot	PhD	09/1977	07/1980	Immunology
Residency training				

A.Personal Statement

My clinical and research activities, as well as those of my group, have focused on the care of patients with glomerular disease and the elucidation of the underlying pathophysiological mechanisms. As Head of the Renal Division (1995–2018) and Director of the INSERM Kidney Research Unit (1998–2018) at Tenon Hospital in Paris, I was able to foster an environment highly conducive to teaching and practicing translational nephrology. Over these years, I have mentored an entire generation of clinical investigators, three of whom have attained full professorships in Paris. In recognition of my contributions to training, I received a Doctor Honoris Causa from Louvain Catholic University for mentoring more than 20 fellows from Belgium, most of whom now hold leadership positions in universities or major clinical institutions in their country. Additionally, I have trained 20 postdoctoral researchers from Japan, China, Europe, and Maghrebian countries, all of whom currently occupy faculty or research positions worldwide.

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This supportive environment also allowed me to host several Visiting Professors, including Daniel MURUVE (2016), now Chief of the Nephrology Department at the University of Calgary Medical Center (Canada), and Bob ATKINS (former President of the International Society of Nephrology) and Prue HILL from the University of Sydney (Australia, 2011–2012).

My group's major contributions to clinical science, kidney immunopathology, and rare kidney diseases have been driven by a close, bidirectional exchange between the clinical division and the research unit. These collaborations enabled us to:

- Identify the first antigen, neutral endopeptidase, involved in a rare subset of neonatal membranous nephropathy, paving the way for the identification of PLA2R, the major antigen in adult membranous nephropathy.
- Discover a new mechanism of maternal-fetal alloimmunization targeting the kidney, expanding beyond previously known incompatibilities involving red blood cells (Rhesus) and platelets.
- Demonstrate the role of a food antigen, bovine serum albumin, in glomerular disease.
- Characterize a new syndrome linked to mutations in the α1 chain of type IV collagen (COL4A1), which we named HANAC (Hereditary Angiopathy with Nephropathy, Aneurysms, and muscular Cramps).

In collaboration with investigators from the Mayo Clinic, we further identified three antigens in pediatric (Semaphorin 3B) and adult membranous nephropathy (NELL-1 and PCDH-7), as well as two biomarkers, Exostosins 1 & 2, specific to lupus membranous nephropathy. Together with Arkana Lab (Little Rock) and Cliniques Saint-Luc in Brussels, we also identified cubilin and amnionless as new antigens in a rare autoimmune disease affecting the proximal tubule.

These advances were made possible by a combination of factors: the large recruitment of patients with rare kidney diseases at Tenon Hospital, strong national and international collaborations with pediatricians, and the proximity of a highly active research unit with a long tradition of translational research. My combined expertise in clinical care, immunology, and kidney pathology provides a unique perspective in the field and has resulted in over 500 research publications, including in *New England Journal of Medicine* (10), *The Lancet* (2), *Science* (2), *Journal of Experimental Medicine* (3), *Journal of Cell Biology* (3), and all major nephrology journals, as well as 30 textbook chapters (Hirsch Index 81, Web of Science;).

Due to my expertise in translational nephrology and commitment to disseminating knowledge at the highest level, the International Society of Nephrology (ISN) invited me to chair or co-chair the Scientific Program Committee for four World Congresses of Nephrology (Madrid, Milan, Cape Town, Mexico). More recently, I was appointed Editor-in-Chief of *Kidney International* (KI) starting January 1, 2018. Under my leadership, the journal's impact factor increased from 8.306 to 18.990 after COVID followed by a decrease to *12.6,*.positioning KI as the leading nephrology journal for original research.

My research has been continuously supported by the French National Research Agency, the Foundation for Medical Research, the Foundation for Rare Diseases, as well as European funding, including the prestigious **ERC Advanced Grant** and collaborative projects (Eunefron, EURenOmics), which enabled the recruitment and mentorship of PhD students and postdoctoral fellows.

B. Positions and Honors

Positions

2018- Emeritus Professor of Nephrology, Sorbonne Université
1998- 2018 Director, Inserm Unit UMR_S 1155, *Rare and common kidney diseases, matrix remodelling and tissue repair*
1995- 2018 Director, Division of Nephrology and Dialysis, Tenon Hospital, Paris, France
1980- 1986 Assistant Professor of Nephrology, Dept. of Nephrology, Tenon Hospital (Gabriel Richet)
2013- President, AURA (Non-profit Association caring 1,500 patients on a dialysis program)
2011- Vice-president, *French Kidney Foundation*
2007-2009 President, *Francophone Society of Nephrology*

Fellowships and awards

2023 *Jean Hamburger Medal*, Francophone Society of Nephrology
2021 Chan Woon Cheung Memorial Fund Award Lecture
2018 Doctor *Honoris Causa*, Université Catholique de Louvain
2016 Honorary Member, Japanese Society o Nephrology
2016 ERA-EDTA Award for *Outstanding Basic Science Contributions to Nephrology*
2012 Advanced Grant *European Research Council*
2012 FERA (ERA-EDTA Distinguished fellow)
2012 *Grand Prix de Médecine et de la Recherche Médicale de la Ville de Paris*
2011 *Jean Dausset* Award (French Society of Immunology)
2011 *Rose Lamarca* Award (French Foundation for Medical Research)
2009 Medal of the Moroccan Society of Nephrology
2008 Senior, then Honorary Member, *Institut Universitaire de France*
2007 *Jean Hamburger award*, International Society of Nephrology

Chair of scientific meetings

2022 President, ERA-EDTA Congress, Paris (10,000 Px)
2018 Co-chair European Rare Kidney Disease Network: Nephropathology Workshop, Paris (150 Px)
2018 Renal Pathology Society meeting, Paris (150 Px*)*
2017-2019 Chair, Theme Gomerulonephritis, World, Congress of Nephrology, Melbourne (8,000 Px)
2016 Co-President, 28th Annual meeting of the ERCSG, Montvillargenne, France (120 Px)
2015-2017 Cochair, Scientific Program Committee, World Congress of Nephrology, Mexico (6,000 Px)
2013-2015 Chair, Scientific Program Committee, World Congress of Nephrology, CapeTown (5000 Px)
2012 President, ERA-EDTA Congress, Paris (12,000 Px)

2012-2017 Co-chair, World Kidney Day, *Académie nationale de médecine*, Paris (150 Px)
2009 President, Scientific Program Committee, Amgen Symposium, Paris, France (200 Px)
2007-2009 Co-chair, SPC, World Congress of Nephrology (ISN/ERA-EDTA), Milan, Italy (10,000 Px)

Institutional responsibilities

International Committees

2018- CK-Net (China Kidney Network) International Advisory Committee
2009-2014 EDTA Inherited Kidney Disorders and Immunopathology Working Groups
2009-2016 ISN Forefronts Committee
2009- Scientific advisory board, NIH network on rare diseases (NEPTUNE)
2009-2014 International Scientific Advisory Board, Dutch Kidney Foundation
2008-2011 Clinical Science Committee, American Society of Nephrology

French Committees

2013-2018 Research Council, *Foundation for Medical Research*
2013-2015 Oversight Committee, *Fondation pour la Recherche Médicale*
2012 -2016 Advisory board, *Foundation IHU, Cardiometabolism and Nutrition Institute* (ICAN)
2012- CKD REIN Study Scientific Committee
2011- Scientific Council *Foundation for Rare Diseases*

Evaluation, editorship and reviewing activities

2018 Peer Review Committee RIHS and RIMLS, Radboud Universiteit, Nijmegen (NL)
2018 **Nominations***:*
Young Investigator Award ASN: A. Greka (Harvard),
Jean Hamburger Award ISN: D. Schlöndorff (NY),
Bywaters Award ISN: Karl Nath (Rochester)
Since 2012- **Promotions**:
CJ. He (Chief, Renal Division of Nephrology, ICAN, NY),
L. Beck (Associate Professor, Boston Univ.),
MB. Stokes (Professor of Pathology, Columbia, NY),
K. Kiryluk (Professor, Columbia, NY)

Editorship

2018- **Editor in Chief, Kidney International**
2007-2017- Theme Editor 'Glomerular Disease' for Nephology Dialysis and Transplantation
1997-2005 Associate Editor, Kidney International
1997-2004 Section Editor, Current Opinion in Nephrology and Hypertension

Editorial Boards

2014- Journal of Kidney Diseases (Zhi-Hong Liu, Hangzhou)
2014-2016 Advisory Board of Seminars in Immunopathology
2007-2017 Journal of the American Society of Nephrology
2007-.2014 Nephron-Experimental Nephrology
2005-2017 Nature Clinical Practice Nephrology/Nature Reviews Nephrology
2002-. Clinical and Experimental Nephrology (Japanese Society of Nephrology)

Reviewing activities: All Nephrology journals, Science, PNAS, JCI, New England Journal of Medicine

C. Contributions to Science

1.Identification of the Angiotensin-2 related idiotypic network

My laboratory initially focused on the idiotypic antibody network of angiotensin II, one of the most potent vasoconstrictors. In two landmark studies with investigators at Johns Hopkins published in *Science*, we demonstrated that anti-idiotypic antibodies could mimic the biological activity of angiotensin II, uncovering a previously unrecognized layer of regulation within the renin–angiotensin system. These findings provided a

conceptual framework linking immunology and cardiovascular physiology, with enduring implications for our understanding of blood pressure regulation and vascular biology.

1.Garcia KC, Desiderio SV, **Ronco PM**, Verroust PJ, Amzel LM. Recognition of angiotensin II: antibodies at different levels of an idiotypic network are superimposable. SCIENCE. 1992 257 :528-31.
2.Garcia KC, **Ronco PM**, Verroust PJ, Brünger AT, Amzel LM. Three-dimensional structure of an angiotensin II-Fab complex at 3 A: hormone recognition by an anti-idiotypic antibody. SCIENCE. 1992 257:502-7.

2. Identification of antigens and risk alleles in membranous nephropathy (MN) and immune-mediated podocytopathies: a paradigm of translational medicine

Membranous nephropathy (MN) is the leading cause of nephrotic syndrome in adults and carries a significant risk of progression to kidney failure. In 2002, we identified neutral endopeptidase (NEP) as the first podocyte antigen responsible for a rare subset of neonatal MN. This discovery represented a major breakthrough, occurring nearly 20 years after Heymann's identification of megalin/LRP2 in the rat model, at a time when most research groups had ceased the search for a human antigen.

The identification of NEP paved the way for the subsequent discovery of M-type phospholipase A2 receptor (PLA2R) and THSD7A antigens by international teams, which account for 70–80% and 1–5% of primary MN cases, respectively. For years, the remaining antigens remained elusive until 2019, when, in collaboration with investigators at the Mayo Clinic (Rochester, USA), we identified Exostosin-1 and Exostosin-2 (EXT1/2) and Neural EGF-like-1 (NELL-1) as antigens in lupus and primary MN, respectively, as well as Semaphorin 3B in pediatric cases. These discoveries have transformed the diagnosis and management of MN, establishing a new paradigm in translational nephrology.

In parallel, we performed the first genome-wide association study (GWAS) in European populations (UK, Netherlands, France) and identified two series of risk alleles in **HLA-DQA1** and **PLA2R1**, the gene encoding the primary target antigen in MN. Using a genetic approach, we further demonstrated that non-coding SNPs in the donor genome are associated with recurrence of MN after kidney transplantation.

Translating these findings to the bedside, we conducted the first clinical trial demonstrating the efficacy of rituximab, an anti-CD20 monoclonal antibody, in achieving both immunological and clinical remission in patients with MN.

Building on these advances in membranous nephropathy, our group extended its focus to immune-mediated podocytopathies. After initially investigating genetic contributions, we served as co-senior authors on a landmark study led by Tobi Huber in Hamburg, published in the *New England Journal of Medicine*. This study demonstrated that anti-nephrin antibodies are detectable in up to 90% of children with steroid-sensitive nephrotic syndrome, 44% of adults with minimal change disease, and 9% of patients with primary focal segmental glomerulosclerosis (FSGS). These findings expand the spectrum of autoimmune podocytopathies and open new avenues for targeted therapeutic interventions.

1.Debiec H, Guigonis V, Mougenot B, Decobert F, Haymann JP, Bensman A, Deschênes G, **Ronco P**. Antenatal membranous glomerulonephritis due to anti-neutral endopeptidase antibodies. N ENGL J MED. 2002 ;346 :2053-60.

2. Debiec H, Lefeu F, Kemper MJ, Niaudet P, Deschênes G, Remuzzi G, Ulinski T, **Ronco P**. Early childhood membranous nephropathy due to cationic bovine serum albumin. N ENGL J MED. 2011;364:2101-102.

3. Debiec H, **Ronco P**. PLA2R autoantibodies and PLA2R glomerular deposits in membranous nephropathy. N ENGL J MED. 2011; 364:689-90.
4. Stanescu HC,et al.....**Ronco P*,** Mathieson PW*, Kleta R*. Risk HLA-DQA1 and PLA(2)R1 alleles in idiopathic membranous nephropathy. N ENGL J MED. 2011 ;364:616-26. *** Co-senior author**
5. Dahan K, Debiec H, Plaisier E, et al,.....**Ronco P**. GEMRITUX Study Group. Rituximab for Severe Membranous Nephropathy: A 6-Month Trial with Extended Follow-Up. J AM SOC NEPHROL. 2017;28:348-358.
6. Hengel FE, et al ....**Ronco P*,** Vivarelli M*, Gesualdo L*, Thomas NM*, Huber T*.Autoantibodies targeting nephrin in podocytopathies. N ENGL J MED 2024;391: 422-433 *** Co-senior author**

3. HANAC: a new genetic syndrome affecting COL4A1

We described a new autosomal dominant syndrome, **Hereditary Angiopathy, Nephropathy, Aneurysms, and Muscle Cramps (HANAC)**, caused by mutations in **COL4A1**, which encodes the α1 chain of type IV collagen,

a key component of basement membranes. Patients with HANAC present with a characteristic constellation of clinical features, including cerebral small vessel disease, retinal tortuosity, muscle cramps, and kidney involvement, which manifests as multiple renal cysts, chronic kidney failure, and occasionally hematuria. Mutations responsible for HANAC localize to the integrin-binding site containing the CB3[IV] fragment of the COL4A1 protein.

To understand the pathogenesis of HANAC, we performed detailed reverse phenotyping by generating genetically modified mice carrying the human mutation. These models allowed us to characterize the molecular and cellular mechanisms underlying kidney, muscle, retinal, and cerebral vascular pathology. Although HANAC is a rare disorder, its study provides important insights into the pathophysiology of more common conditions affecting the same organs, including diabetes, cachexia, and neurovascular diseases.

1. Plaisier E, Gribouval O, Alamowitch S, Mougenot B, Prost C, Verpont MC, Marro B, Desmettre T, Cohen SY, Roullet E, Dracon M, Fardeau M, Van Agtmael T, Kerjaschki D, Antignac C, **Ronco P**__COL4A1 mutations and hereditary angiopathy, nephropathy, aneurysms, and muscle cramps. N ENGL J MED 2007; 357:2687-95.
2. Alamowitch S, Plaisier E, Favrole P, Prost C, Chen Z, Van Agtmael T, Marro B, **Ronco P**. Cerebrovascular disease related to COL4A1 mutations in HANAC syndrome. NEUROLOGY. 2009 ;73:1873-82
3. Chen Z, Migeon T, Verpont MC, Zaidan M, Sado Y, Kerjaschki D, **Ronco P**, Plaisier E.. HANAC Syndrome Col4a1 Mutation Causes Neonate Glomerular Hyperpermeability and Adult Glomerulocystic Kidney Disease. J AM SOC NEPHROL 2016, 27:1042-54
4. Plaisier E, **Ronco P**. COL4A1-Related Disorders 2009 Jun 25 [updated 2016 Jul 7]. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GENE REVIEWS®

D. Research Support (Last 10 years)

Project Title	*Funding source*	*Amount (Euros)*	*Period*	*Role of the PI*
OSAI " Membranous nephropathy : a model for solving organ-specific auto-immunity"	**European Research Council**	**2 500 000**	**From May 1st, 2013 to April 30th, 2019**	**Research coordination**
MN-Aims " Molecular dissection of PLA2R1-related membranous nephropathy: towards a portfolio of new clinical biomarkers "	National Research Agency (ANR)	249 921	From October 1st, 2017 to November 30th, 2020	Research coordination
Genetransnephrose " Genetic and translational studies in patients with steroid sensitive nephrotic syndrome (SSNS)"	National Research Agency (ANR)	528 518	From October 1st, 2016 to September 30th, 2021	Research coordination
"Impact of anti-C5 antibody on proteinuria in an in vivo model of membranous nephropathy"	Alexion	222 300	From December 19th, 2017 to June 18th, 2019	Research coordination
SeroNegMN "PLA2R-negative membranous nephropathy: antigens, models and patients"	National Research Agency (ANR)	392000	From October 1st, 2020 to September 30th, 2023	Research coordination
AirMN **"**Dynamics of anti-PLA2R1 and anti-THSD7A antibodies in patients with membranous nephropathy: from early stages to active disease"	National Research Agency (ANR)	64900	From October 1st, 2020 to September 30th, 2024	Partner

I have obtained 2 more grants from the National Research Agency in 2024 (Antibody-mediated primary nephrotic syndrome: a paradigm shift for diagnosis and prognostication (NEPHROSIN) & 2025 (PLA2R1-associated membranous nephropathy: From pathophysiology to new therapies) both as a Partner (ongoing financial negotiation)

NEJM Publications (Senior author of 8/10)

1. Hengel FE, Dehde S, Lassé M, et al, **Ronco P*,** Vivarelli M*, Gesualdo L*, Tomas NM*, Huber TB*****; **International Society of Glomerular Disease***.* Autoantibodies Targeting Nephrin in Podocytopathies. *N Engl J Med.* **2024**;391:422–433. ****Co-senior authors***
   Identified anti-nephrin autoantibodies driving steroid-sensitive nephrotic syndrome, minimal change disease, and selected FSGS; expanded understanding of immune podocytopathies.
2. Seikrit C**, Ronco P,** Debiec H. Factor H Autoantibodies and Membranous Nephropathy. *N Engl J Med.* **2018**;379:2479–2481.
   Demonstrated complement dysregulation via factor H autoantibodies, broadening immunopathological insights in membranous nephropathy.
3. Boyer O, Nevo F, Plaisier E, et al**.; Ronco P.** INF2 Mutations in Charcot–Marie–Tooth Disease with Glomerulopathy. *N Engl J Med.* **2011**;365:2377–2388.
   Linked peripheral neuropathy and glomerular disease through INF2 mutations, highlighting actin cytoskeleton regulation in podocyte function.
4. Debiec H, Lefeu F, Kemper MJ, et al.; **Ronco P.** Early-Childhood Membranous Nephropathy due to Cationic Bovine Serum Albumin. *N Engl J Med.* **2011**;364:2101–2110.
   Proved that exogenous antigens can trigger pediatric membranous nephropathy, clarifying disease mechanisms.
5. Debiec H**, Ronco P.** PLA2R Autoantibodies and PLA2R Glomerular Deposits in Membranous Nephropathy. *N Engl J Med.* **2011**;364:689–690.
   Confirmed pathogenic relevance of anti-PLA2R antibodies and glomerular deposition; reinforced antigen-specific diagnostics.
6. Stanescu HC, Arcos-Burgos M, Medlar A, et al.; Wetzels J*, **Ronco P*,** Mathieson P*, Kleta R* Risk HLA-DQA1 and PLA2R1 Alleles in Idiopathic Membranous Nephropathy. *N Engl J Med.* **2011**;364:616–626.***Co-senior authors****.*
   Established genetic susceptibility alleles underpinning autoimmunity in membranous nephropathy.
7. Plaisier E, Gribouval O, Alamowitch S, et al.; **Ronco P.** COL4A1 Mutations and HANAC Syndrome. *N Engl J Med.* **2007**;357:2687–2695.
   Described a novel autosomal dominant syndrome caused by COL4A1 mutations, revealing systemic effects of basement membrane defects.
8. Jaccard A, Moreau P, Leblond V, et al.; **Ronco P.** High-Dose Melphalan vs Melphalan plus Dexamethasone for AL Amyloidosis. *N Engl J Med.* **2007**;357:1083–1093.
   Randomized trial informing AL amyloidosis treatment strategies, emphasizing renal involvement.
9. Debiec H, Guigonis V, Mougenot B, et al.; **Ronco P.** Antenatal Membranous Glomerulonephritis due to Anti–Neutral Endopeptidase Antibodies. *N Engl J Med.* **2002**;346:2053–2060.
   First identification of a podocyte antigen causing antenatal membranous nephropathy; initiated antigen-based classification.
10. **Ronco P,** Flahault A**.** Drug-Induced End-Stage Renal Disease. *N Engl J Med.* **1994**;331:1711–1712.
    Early analysis highlighting iatrogenic contributions to irreversible kidney failure and long-term outcomes.