



### BIOGRAPHICAL SKETCH

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NAME: Cattaneo, Elena

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Full Professor of Pharmacology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION           | DEGREE<br>(if<br>applicable) | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY                           |
|------------------------------------|------------------------------|-------------------------------|------------------------------------------|
| University of Milan (Milan, Italy) | Laurea<br>degree             | 07/1986                       | Pharmacology                             |
| University of Milan (Milan, Italy) | Doctorate                    | 1991                          | Biotechnology Applied<br>to Pharmacology |

#### A. Personal Statement

I am the director of the “Laboratory of Stem Cell Biology and Pharmacology of Neurodegenerative Diseases” at the Department of Biosciences, as well as the co-founder and Director of UniStem, the Centre for Stem Cell Research at the University of Milan. Since 2015, the University has established a partnership with the National Institute of Molecular Genetics (INGM), and now my lab is hosted by INGM.

I was born in Milan and earned a PhD in Biotechnology Applied to Pharmacology at the University of Milan. I spent a few years in Boston at the Massachusetts Institute of Technology, where I studied neural stem cell differentiation in the area of the human brain associated with degenerative diseases, under the supervision of Professor Ronald McKay. I have also joined for a brief period Professor Anders Bjorklund’s lab at Lund University, where I learned grafting techniques of stem cells. Back to Italy, I became researcher in 1995, Associate Professor in 2001 and Full Professor in 2003.

The main focus of my lab is the molecular pathophysiology and treatment of Huntington’s Disease (HD). Using genetically precise cell and animal models, we aim to better understand the events leading to striatal neurodegeneration. One approach involves using embryonic stem cells technologies to obtain the medium-sized spiny striatal neurons that degenerate in HD and develop cell platforms to study HD mechanisms. Ongoing studies of human foetal striatum development in vivo through single-cell RNA-seq analysis aim to improve the differentiation of striatal neurons in vitro. These cells are used for experimental transplantation studies. In parallel we are interested at



testing whether there is developmental component in HD. Our research also examines the role of cholesterol and synaptic signaling pathways in HD. Another area of focus is the function and evolution of the normal huntingtin gene, with the ultimate goal of identifying cells, molecules, and pathways for therapeutic intervention in Huntington's Disease.

Over the years, my lab has received funding from organizations like the Huntington's Disease Society of America, the Hereditary Disease Foundation, the CHDI Foundation (New York), the European Commission (FP7, H2020), the Ministry of Research and University in Italy (PRIN), the Fondazione Telethon and many others. I have coordinated three EU-funded research consortia (including NeuroStemCell 2008-2012, NeuroStemCell-Repair 2013-2017, and, currently, NeuroStemCell-Reconstruct 2019-2024), and I also lead an Italian network on stem cell transplantation for Huntington's Disease funded by the Ministry of Research and University. In 2018 I was awarded an Advanced ERC Grant and in 2024 the ERC Synergy Grant alongside three colleagues. The grant agreement is currently in preparation and is scheduled to begin in 2025. As part of the CHDI-funded grant which started in 2016 and was completed in June 2024, we began testing the hypothesis that HD may exhibit transcriptional alterations during fetal development. We performed single-cell RNA-seq on fetal mouse and human cortex and striatum samples from both control and HD cases (with only one human HD fetal sample available). These studies did not include any spatial transcriptomic analyses, as they were beyond our capabilities at the time. Nevertheless, we have already generated a substantial amount of single-cell omics data.

I have published more than 200 papers in peer-reviewed journals such as *Science*, *Nature*, and *Journal of Neuroscience*. My H index is 65. I have also taught several courses, including "Stem Cells in Pharmacology and in Regenerative Medicine" at the University of Milan. Since my appointment as Senator for Life in 2013, I no longer hold formal courses, but I still lecture in courses held by my colleagues. I have supervised more than 130 PhD and Master's students. I have been invited to give over 400 lectures around the world. I am also deeply engaged in organizing professional development and outreach events for both the scientific community and the general public.

In 2006, I co-founded and became the Director of UniStem, which focuses on stem cell research and outreach. We organize several events, including scientific workshops, keynote lectures, and a national event dedicated to high school students, reaching over 25,000 students from more than 90 Italian and European universities.

I was appointed as a Senator for Life by President Giorgio Napolitano for scientific and social merit, I happen to be the youngest and the third woman in Italian history to hold this position. In the Senate, I focus on science, innovation, research freedom, human rights, and education.

## **B. Positions, Scientific Appointments, and Honors**

### *Current positions*

2006-current Co-founder and Director of UniStem, Centre for Stem Cell Research, Univ. of Milan  
2003-current Full Professor of Pharmacology at the University of Milan  
1995-current Director, Laboratory of Stem Cell Biology and Pharmacology of Neurodegenerative Diseases, Department of Biosciences, University of Milan

### *Previous positions*

2001 Associate Professor at the University of Milan  
1995 Assistant Professor (tenure track position), University of Milan  
1993 Fellowship sponsored by the Hereditary Disease Foundation, which allowed me to set up a group at the Department of Pharmacological Sciences, University of Milan  
1992 Research stage (cumulative of 6 months) at the University of Lund, Sweden (P.I.)



- 1989-1992 Prof. Anders Bjorklund; working on intracerebral cell transplantation)  
Research Fellow, Department of Brain and Cognitive Sciences M.I.T., Cambridge, USA (P.I. Prof. Ronald McKay; working on neural stem cells)
- 1987-1988 Research Fellow, Department of Pharmacological Sciences, University of Milan (P.I. Prof. A. Maggi; working on estrogens in brain)
- 1985-1986 Research training at Recordati Pharmaceutical S.P.A. focused on Calcium antagonists for the preparation of the Laurea thesis (P.I. Dr. A. Abbiati)

*Honours and awards (selection)*

- 2021 Leslie Gehry Brenner Prize – Hereditary Disease Foundation, USA
- 2019 Honorary Member of National Academy of Agriculture
- 2018 *Honorary Doctor* in Medicine, Lund University (Sweden)
- 2014 Public Service Award, International Society for Stem Cell Research ISSCR, USA
- 2013 Member of Accademia dei Lincei, Roma (Italy)
- 2013 Member of European Molecular Biology Organization EMBO
- 2009 Member of ISSCR Task Force on *Unproven Stem Cell Therapies*, USA
- 2008 Grande Ippocrate Prize “Medical researcher of the year”, Unamsi & Novartis Pharma
- 2006 Knighted by the President of the Italian Republic, Hon. Carlo Azeglio Ciampi
- 2001 Gold Medal from the President of the Republic Hon. Carlo Azeglio Ciampi
- 1991,1992 Fellowship from the Hereditary Disease Foundation, USA

**C. Contributions to Science**

*Selection of the most relevant and recent peer-reviewed publications:*

Maestri S., Scalzo D., Damaggio G., Zobel M., Besusso D., Cattaneo E. (2024) Navigating triplet repeats sequencing: concepts, methodological challenges and perspective for Huntington's disease. **Nucleic acids research**, gkae1155. Advance online publication. doi: 10.1093/nar/gkae1155

Cattaneo E., Scalzo D., Zobel M., Iennaco R., Maffezzini C., Besusso D., Maestri S. (2024) When repetita no-longer iuvant: somatic instability of the CAG triplet in Huntington's disease. **Nucleic acids research**, gkae1204. Advance online publication. doi: 10.1093/nar/gkae1204

Cattaneo E., Barker R. A. (2024) Brain cholesterol therapy for Huntington's disease - Does it make sense?. **Clinical and translational medicine**, 14(7):e1746. doi: 10.1002/ctm2.1746

Galimberti M., Nucera M. R., Bocchi V. D., Conforti P., Vezzoli E., Cereda M., Maffezzini C., Iennaco R., Scolz A., Falqui A., Cordiglieri C., Cremona M., Espuny-Camacho I., Faedo A., Felsenfeld D. P., Vogt T. F., Ranzani V., Zuccato C., Besusso D., Cattaneo E. (2024) Huntington's disease cellular phenotypes are rescued non-cell autonomously by healthy cells in mosaic telencephalic organoids. **Nature communications**, 15(1):6534. doi: 10.1038/s41467-024-50877-x

Valenza M., Birolini G., Cattaneo E. (2023) The translational potential of cholesterol-based therapies for neurological disease. **Nat Rev Neurol**, 19(10):583-598. doi: 10.1038/s41582-023-00864-5



Schellino R., Besusso D., Parolisi R., Gómez-González G.B., Dallere S., Scaramuzza L., Ribodino M., Campus I., Conforti P., Parmar M., Boido M., Cattaneo E.\*, Buffo A.\* (2023) hESC-derived striatal progenitors grafted into a Huntington's disease rat model support long-term functional motor recovery by differentiating, self-organizing and connecting into the lesioned striatum. **Stem Cell Res Ther**, 14(1):189. doi: 10.1186/s13287-023-03422-4; \* co-last author

Conforti, P.\*, Bocchi, V. D.\*, Campus, I., Scaramuzza, L., Galimberti, M., Lischetti, T., Talpo, F., Pedrazzoli, M., Murgia, A., Ferrari, I., Cordiglieri, C., Fasciani, A., Arenas, E., Felsenfeld, D., Biella, G., Besusso, D., Cattaneo, E. (2022) *In vitro*-derived medium spiny neurons recapitulate human striatal development and complexity at single-cell resolution. **Cell reports methods**, 2(12):100367. doi: 10.1016/j.crmeth.2022.100367 (\*co first authors)

Birolini G.\*, Valenza M.\*, Ottonelli I., Talpo F., Minoli L., Cappelleri A., Bombaci M., Caccia C., Leoni V., Passoni A., Favagrossa M., Nucera M.R., Colombo L., Paltrinieri S., Bagnati R., Duskey J.T., Caraffi R., Vandelli M.A., Taroni F., Salmona M., Scanziani E., Biella G., Ruozi B., Tosi G., Cattaneo E. (2022) Chronic cholesterol administration to the brain supports complete and long lasting cognitive and motor amelioration in Huntington's disease. **Pharmacological Research**, 194:106823. doi: 10.1016/j.phrs.2023.106823 (\*co first authors)

Badin A. R., Lévi A. C. B., Bauer G., Morris M. B., Canals J. M., Capetian P., Cattaneo E., Chen J., Cozzi E., Ellederova Z., Goldman S. A., Gray W., Lai L., Li M., Morenkova A., Pan G., Pei Z., Martin U. P., Perrier A., Reidling J. C., Rosser A. E., Song J., Thompson L. M., Wheelockx V. (2021) Stem Cells for Huntington's Disease (SC4HD): An International Consortium to Facilitate Stem Cell Based Therapy for Huntington's Disease. **Journal of Huntington's Disease**, 10(2):221-226 (Impact Factor 1.081)

Bocchi V.D., Conforti P., Vezzoli E., Besusso D., Cappadona C., Lischetti T., Galimberti M., Ranzani V., Bonnal R.J.P., De Simone M., Rossetti G., He X., Kamimoto K., Espuny Camacho I., Faedo A., Gervasoni F., Vuono R., Morris S.A., Chen J., Felsenfeld D., Pavesi G., Barker R.A., Pagani M., Cattaneo E. (2021) The coding and long noncoding single cell atlas of the developing human fetal striatum. **Science** 2021 May 7;372(6542):eabf5759 (Impact Factor 41,85)

Birolini G., Verlengia G., Talpo F., Maniezzi C., Zentilin L., Giacca M., Conforti P., Cordiglieri C., Caccia C., Leoni V., Taroni F., Biella G., Simonato M., Cattaneo E., Valenza M. (2021) SREBP2 gene therapy targeting striatal astrocytes ameliorates Huntington's disease phenotypes. **Brain**, 144(10):3175-3190. PMID: 33974044 (Impact factor 11,34)

Rivetti di Val Cervo P., Besusso D., Conforti P., Cattaneo E. (2021) hiPSCs for predictive modelling of neurodegenerative diseases: dreaming the possible. **Nature Reviews Neurology**, 17(6):381-392 (Impact Factor 27, Cit. n/a)

Birolini G., Valenza, M., Ottonelli, I., Passoni, A., Favagrossa, M., Duskey, J. T., Bombaci, M., Vandelli, M. A., Colombo, L., Bagnati, R., Caccia, C., Leoni, V., Taroni, F., Forni, F., Ruozi, B., Salmona, M., Tosi, G., Cattaneo, E. (2021). Insights into kinetics, release, and behavioral effects of brain targeted hybrid nanoparticles for cholesterol delivery in Huntington's disease. **Journal of controlled release: official journal of the Controlled Release Society**, 330:587-598. (Impact Factor 7.727, Cit. n/a)



Conforti P., Besusso D., Brocchetti S., Campus I., Cappadona C., Galimberti M., Laporta A., Iennaco R., Rossi R.L., Dickinson V.B., Cattaneo E. (2020) RUES2 hESCs exhibit MGE biased neuronal differentiation and muHTT dependent defective specification hinting at SP1. **Neurobiology of Disease**, 146:105140 (Impact Factor 5.332, Cit. n/a)

Birolini G., Valenza M., Di Paolo E., Vezzoli E., Talpo F., Maniezzi C., Caccia C., Leoni V., Taroni F., Bocchi V.D., Conforti P., Sogne E., Petricca L., Cariulo C., Verani M., Caricasole A., Falqui A., Biella G., Cattaneo E. (2020) Striatal infusion of cholesterol promotes dose dependent behavioral benefits and exerts disease modifying effects in Huntington's disease mice. **EMBO Molecular Medicine**, 12(10):e12519 (Impact Factor 8.800; Cit. 1)

Besusso D., Cossu A., Mohamed A., Cernigoj M., Codega P., Galimberti M., Campus I., Conforti P., Cattaneo E. (2020) A CRISPR strategy for the generation of a detectable fluorescent hESC reporter line (WAe009 A 37) for the subpallial determinant GSX2. **Stem Cell Research**, 49:102016 (Impact factor 6.032; Cit. n/a)

Besusso D., Schellino R., Boido M., Belloli S., Parolisi R., Conforti P., Faedo A., Cernigoj M., Campus I., Laporta A., Bocchi V.D., Murtaj V., Parmar M., Spaiardi P., Talpo F., Maniezzi C., Toselli M., Biella G., Moresco R.M., Vercelli A., Buffo A., Cattaneo E. (2020) Stem cell derived human striatal progenitors innervate striatal targets and alleviate sensorimotor deficit in a rat model of Huntington Disease. **Stem Cell Reports**, 14(5):876-891

Conforti P., Besusso D., Bocchi VD, Faedo A., Cesana E., Rossetti G., Ranzani V., Svendsen CN, Thompson LM, Toselli M., Biella G., Pagani M., Cattaneo E., (2018) Faulty Neuronal determination and cell polarization are reverted by modulating HD early phenotypes. **Proceedings of the National Academy of Sciences USA**, 115(4):E762-E771

Faedo A., Laporta A., Segnali A., Galimberti M., Besusso D., Cesana E., Belloli S., Moresco RM, Tropiano M., Fucà E., Wild S., Bosio A., Vercelli AE, Biella G., Cattaneo E. (2017) Differentiation of human telencephalic progenitor cells into MSNs by inducible expression of Gsx2 and Ebf1. **Proceedings of the National Academy of Sciences USA**, 114(7):E1234-E1242