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# ANTONINO CATTANEO

**Presidente**

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After obtaining a degree in biophysics, Antonino Cattaneo worked as a PhD student at the Scuola Normale Superiore (Pisa) with Lamberto Maffei and as a postdoc and staff scientist with Rita Levi-Montalcini (Nobel Laureate for the discovery of NGF) at the CNR Institute of Neurobiology in Rome. He later worked with Cesar Milstein (Nobel Prize laureate for the discovery of monoclonal antibodies) and Michael Neuberger at the MRC Laboratory of Molecular Biology (Cambridge, UK).

From 1991 to 2008, he was Full Professor of Biophysics at the International School for Advanced Studies (SISSA) in Trieste (Italy), where he was Head of the Biophysics Department from 1991 to 1995 and the Deputy Director of SISSA from 1996 to 2001. Since 2008 he is Professor of Neurobiology at the Scuola Normale Superiore (Pisa), where he is also the Director of the Biology Lab Bio@SnS.

Antonino Cattaneo is author of more than 200 publications in peer-reviewed international scientific journals and is recipient of several awards including Domenico Marotta Prize (Accademia Nazionale delle Scienze detta XL), the W. Jansenius Medal (Slovak Academy of Sciences) and the "G. Tartufari" International Prize for Biology (Accademia Nazionale dei

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Lincei). He is a member of EMBO (European Molecular Biology Organization) and member of the Accademia Nazionale delle Scienze detta XL, the Accademia Europaea and of the Accademia Nazionale dei Lincei.

Since 2018 he is President of the European Brain Research Institute 'Rita Levi-Montalcini'.

### **Positions held**

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| 2018 to present | President of the European Brain Research Institute 'Rita Levi-Montalcini'                         |
| 2008 to present | Full Professor of Physiology, and Director of Bio@SNS Laboratory, Scuola Normale Superiore (Pisa) |
| 1995-1997       | PI at MRC Laboratory of Molecular Biology (Cambridge, UK) (sabbatical leave from SISSA)           |
| 1991-2008       | Full Professor of Biophysics (SISSA, Trieste)   |
| 1987-1991       | Associate Professor (University of Naples) and Group Leader at the CNR Institute of Neurobiology  |
| 1985 -87        | MRC Laboratory of Molecular Biology (Cambridge), with Cesar Milstein and Michael Neuberger        |
| 1980-1985       | CNR Institute of Neurobiology, Post doc with Rita Levi-Montalcini and Pietro Calissano            |
| 1977-1980       | Scuola Normale Superiore (Pisa) PhD student with Lamberto Maffei                                  |
| 1976            | University of Rome La Sapienza, Degree in Physics (Thesis supervisor Mario Ageno)                 |

### **Directorial and scientific management positions:**

President of the Rita Levi-Montalcini EBRI Foundation (2018 to present)

Head of Biophysics Sector, SISSA (1991-1995)

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Deputy Director, SISSA (1997-2000)

He was directly involved in building from scratch the Neuroscience Program at SISSA and the Rita Levi-Montalcini European Brain Research Institute (EBRI).

### **Awards and Honors**

Member of European Molecular Biology Organization (EMBO)

Member of the Accademia Nazionale delle Scienze dei XL

Member of the Accademia Nazionale dei Lincei

Life member of Clare Hall College (Cambridge)

Visiting Fellow Commoner of Trinity College (Cambridge)

Chairman of the Human Frontier Science Program Review Committee (Brain) 1997-2000

Prizes include the Domenico Marotta Prize (Accademia Nazionale delle Scienze dei XL), the W. Jansenius Medal (Slovak Academy of Sciences), the G. Tartufari International Prize for Biology (Accademia Nazionale dei Lincei).

### **Research activity**

Cattaneo's research has been highly innovative and imaginative, with pioneering findings and novel methods, which opened new fields. He made seminal contributions to the fields of neurotrophins and of Alzheimer's disease, as well as to the field of recombinant antibodies. He pioneered protein interference with antibody genes and by this approach he established a new neurodegeneration mechanism, whereby deficits in proNGF/NGF signaling in the adult brain induce a progressive neurodegeneration that phenocopies Alzheimer's disease. This underpins innovative therapeutic approaches for AD currently under development towards clinical testing: painless NGF. His antibody technologies led to two therapeutic antibodies under clinical development in man for chronic pain and to a humanized nanobody against intracellular A<sub>β</sub> oligomers that is being developed for Alzheimer's disease. He established Synactive, a new method for the activity-dependent

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local expression of optogenetic probes at potentiated synapses in vivo and is using it to study synaptic memory engrams in physiology and pathology.

His work has also a strong translational impact with clinical potential, testified by several granted patents. His papers received over 14500 quotations, H index = 64 (i10-index = 196).

Main achievements:

i) the discovery that neutralizing NGF signaling in the adult mouse brain induces a progressive neurodegeneration that phenocopies human Alzheimer's disease, encompassing cholinergic deficit, tau hyperphosphorylation and activation of amyloidogenic APP processing to form A $\beta$ , providing a causal link between alterations in NGF signalling/processing and the activation of Alzheimer's neurodegeneration

ii) the discovery that proNGF/NGF unbalance is an upstream driver of Alzheimer's neurodegeneration, and establishing NGF as a neuroprotective modulator of neuroinflammation via microglial cells

iii) this new mechanism underpins the development of "painless NGF", a non invasive NGF-based therapeutic approach to Alzheimer's disease. "Painless NGF", inspired by the pain insensitivity HSAN V genetic disease, is currently developed towards clinical testing in man.

iv) the discovery of neuronal activity-dependent dendritic targeting of BDNF and TrkB mRNA in neurons and of the BDNF/TrkB local synaptic autocrine loop as a synaptic tag for plasticity

v) the development and humanization of therapeutic antibodies (anti NGF and anti TrkA) that are currently in clinical trials in man for chronic pain.

vi) Cattaneo has pioneered a protein interference strategy (intrabodies), whereby the ectopic expression of antibody genes, in cells or tissues, is used to interfere with cellular functions, creating experimental models for mechanistic studies. In this seminal approach, antibodies are used as genes, rather than as proteins. Protein interference with antibodies allows addressing questions that nucleic acid-based methods do not allow (such as conformational-specific and post-translational specific intrabodies).

vii) Synaptic engrams: the development of SYNACTIVE, a new method for the activity-dependent local expression of optogenetic probes at potentiated synapses in vivo, that allows to map potentiated synapses in the brain and to study the necessity and sufficiency of synaptic engrams in physiological and pathological conditions.

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viii) Demonstration of conformation-selective interference against intracellular A $\beta$  oligomers in neurons and in Alzheimer's mice.

## SHORTLIST OF PUBLICATIONS

Biocca S, Neuberger MS, Cattaneo A (1990) Expression and targeting of intracellular antibodies in mammalian cells. *EMBO J* 9:101-108.

Piccioli P, Ruberti F, Biocca S, Di Luzio A, Werge TM, Bradbury A, Cattaneo A (1991) Neuroantibodies: molecular cloning of a monoclonal antibody against substance P for expression in the central nervous system. *Proc Natl Acad Sci U S A* 88:5611-5615.

Tavladoraki P, Benvenuto E, Trinca S, De Martinis D, Cattaneo A, Galeffi P (1993) Transgenic expressing a functional single-chain Fv antibody are specifically protected from virus attack. *Nature* 366:469-472.

Bradbury A, Persic L, Werge T, Cattaneo A (1993) Use of living columns to select specific phage antibodies. *Nature Biotechnology* 11:1565-1569.

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Biocca S, Pierandrei-Amaldi P, Campioni N and Cattaneo A (1994) Intracellular immunization with cytosolic recombinant antibodies. *Nature Biotechnology* 12:396-399.

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Biocca S, Ruberti F, Tafani M, Pierandrei-Amaldi P and Cattaneo A (1995) Redox state of single chain Fv fragments targeted to the endoplasmic reticulum, cytosol and mitochondria. *Nature Biotechnology* 13:1110-1115.

Tongiorgi E, Righi M, Cattaneo A (1997) Activity-dependent dendritic targeting of BDNF and TrkB mRNAs in hippocampal neurons. *J Neurosci* 17:9492-9505.

Righi M, Tongiorgi E and Cattaneo A (2000) Brain-derived neurotrophic factor (BDNF) induces dendritic targeting of BDNF and tyrosine kinase B mRNAs in hippocampal neurons through a phosphatidylinositol-3 kinase-dependent pathway. *J Neurosci* 20:3165-3174.

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Visintin M, Tse E, Axelson H, Rabbitts TH, Cattaneo A (1999) Selection of antibodies for intracellular function using a two-hybrid in vivo system. *Proc Natl Acad Sci U S A* 96:11723-11728.

Pesavento E, Margotti E, Righi M, Cattaneo A, Domenici L (2000) Blocking the NGF-TrkA interaction rescues the developmental loss of LTP in the rat visual cortex: role of the cholinergic system. *Neuron* 25:165-175.

Capsoni S, Ugolini G, Comparini A, Ruberti F, Berardi N, Cattaneo A (2000) Alzheimer-like neurodegeneration in aged anti-nerve growth factor transgenic mice. *Proc Natl Acad Sci U S A* 97:6826-6831.

Capsoni S, Giannotta S, Cattaneo A (2002) Nerve growth factor and galantamine ameliorate early signs of neurodegeneration in anti-nerve growth factor mice. *Proc Natl Acad Sci U S A* 99:12432-12437.

De Rosa R, Garcia AA, Braschi C, Capsoni S, Maffei L, Berardi N, Cattaneo A (2005) Intranasal administration of nerve growth factor (NGF) rescues recognition memory deficits in AD11 anti-NGF transgenic mice. *Proc Natl Acad Sci U S A* 102:3811-3816.

Ugolini G, Marinelli S, Covaceuszach S, Cattaneo A, Pavone F (2007) The function neutralizing anti-TrkA antibody MNAC13 reduces inflammatory and neuropathic pain. *Proc. Natl Acad Sci USA* 104: 2985-2990.

Capsoni, S., Tiveron, C., Amato, G., Vignone, D., Cattaneo, A. (2010) Dissecting the involvement of Tropomyosin kinase A and p75 neurotrophin receptor signaling in NGF deficit-induced neurodegeneration. *Proc Natl Acad Sci USA* 107: 12299-12304.

Tiveron C et al (2013) proNGF/NGF imbalance triggers learning and memory deficits, neurodegeneration and spontaneous epileptic-like discharges in transgenic mice. *Cell Death and Differ.*, 20(8):1017-30. doi: 10.1038/cdd.2013.22

Meli G, Lecci A, Manca A, Krako N, Albertini V, Benussi L, Ghidoni R, Cattaneo A. (2014) Conformational targeting of intracellular A $\beta$  oligomers demonstrates their pathological oligomerization inside the endoplasmic reticulum. *Nature Commun.* 2014 May 27;5:3867. doi: 10.1038/ncomms4867. Highlighted in Alzforum.org.

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Chirichella M, Lisi S, Fantini M, Goracci M, Calvello M, Brandi R, Arisi I, D'Onofrio M, Di Primio C, Cattaneo A. (2017) Post-translational selective intracellular silencing of acetylated proteins with de novo selected intrabodies. *Nat Methods*. 2017 Mar;14(3):279-282. doi: 10.1038/nmeth.4144. Highlighted and commented in *Biocentury*.

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Antonino Cattaneo co-authored the 6<sup>th</sup> edition of the Neuroscience classic textbook *From neuron to Brain (the Nicholl's)*: A. Robert Martin, David A. Brown, Mathew E. Diamond, Antonino Cattaneo, Francisco F. De-Miguel, and Foreword by John Nicholls (2020). *From Neuron to Brain (Volume, sixth edition)* ISBN: 9781605354392, Hardcover, 912 pages, Oxford University Press.