Universidad de Jaén

Investiture of

His Excellency Mr. Thomas C. Südhof

as Doctor *Honoris Causa*

LAUDATIO

Delivered by

Prof. Dr. D. Diego Franco Jaime

Full Professor of the Area of Cell Biology

INVESTITURE SPEECH

By

His Excellency Mr. Thomas C. Südhof

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LAUDATIO

Dear Rector Magnificus of the University of Jaén,
Dear Professor Thomas Südhof,
Dear members of the University of Jaén Governing Council, Deans, and Directors
Dear authorities
Dear professors and students of the University of Jaén
Ladies and Gentlemen

It is a great honor and pleasure for me to be here today, presenting Professor Thomas Südhof to this faculty of doctors as a Doctor Honoris Causa candidate at the University of Jaén. I am sure this honor is also shared by all members of our University.

I will now briefly outline the academic, research, and professional career of Dr. Thomas Südhof, one of the most influential and respected scientists in the field of neuroscience today.

Thomas Südhof was born in Göttingen, Germany, in December 1955. He studied Medicine at the University of Göttingen, graduating in 1982. He subsequently completed his doctoral thesis at the Max-Planck Institute for Byophysical Chemistry (*Max-Planck-Institut für Biophysikalische Chemie*) in Göttingen, under the supervision of Dr. Victor P. Whittaker. His work focused on elucidating the structure of the secretory granules of the chromaffin cells that release adrenaline.

After obtaining his doctorate, Thomas Südhof moved to the United States in 1983 to continue his postdoctoral training at the University of Texas Southwestern Medical Center (*UT Southwestern*) in Dallas, specifically in the Department of Molecular Genetics, where he worked with Dr. Michael S. Brown and Dr. Joseph L. Goldstein. During that time, he contributed to characterizing the regulation of the LDL receptor, i.e., the low-density lipoprotein receptor, as well as to several other regulatory elements of sterol metabolism. It is important to highlight that Prof. Südhof had only been for two years with the laboratory when his supervisors, Drs. Michael S. Brown and Joseph L. Goldstein, received the Nobel Prize in Medicine or Physiology for their pioneering work in the understanding of cholesterol metabolism, in 1985. In 1986, Thomas Südhof began his

independent career at *UT Southwestern*. At that time, he reoriented his research, moving from lipid metabolism to molecular neuroscience, focusing his attention on nerve terminals. These terminals release chemicals called neurotransmitters, which act at highly specialized points of communication between neurons: synapses. Proper brain function depends on the precision of this synaptic communication, a failure of which can lead to psychiatric disorders and neurodegenerative diseases.

During this period, he identified the function of key proteins such as synaptotagmin, a protein that is an essential calcium sensor for the rapid release of neurotransmitters, and discovered multiple components and regulators of the vesicular fusion machinery such as different proteins of the Munc and RIMs families, respectively, which act as scaffolding proteins in the presynaptic active zone, thus helping the neurotransmitter release. He also established their functional relationship with the SNARE complex. Almost three decades ago, his laboratory discovered neurexins and neuroligins, proteins that would later be revealed to be altered synaptic adhesion molecules in autism patients. Since then, Thomas Südhof has been investigating how synapses form, enabling the

establishment of the specific connections that build neural circuits.

In 1998, after a period combining various positions, he accepted the position of director of the Center for Basic Neuroscience at UT Southwestern, Dallas, which later became the Department of Neuroscience few years later. Professor Südhof was, in practice, the founder and driving force behind the department, and held various academic and management responsibilities until his departure to Stanford. His time in Dallas can be defined as decisive both for his molecular discoveries and for his organizational leadership.

It is worth noting that, since 1986, Thomas Südhof has been an investigator at the prestigious Howard Hughes Medical Institute (HHMI), a position that, since the beginning of his independent career, has provided him with the stability and intellectual freedom required to develop far-reaching research programs. Thanks to this, he has trained numerous students and postdoctoral scientists, consolidating a true scientific school of researchers who integrate molecular genetics, biochemistry, and neurophysiology and who now direct scientific laboratories and institutions in the United States, Europe, and Asia. Furthermore, during his time

at the University of Texas Southwestern, he accumulated important awards and recognitions.

In 2008, Prof. Thomas Südhof moved his laboratory to Stanford University in California, where it remains today. At Stanford, Thomas Südhof holds the Avram Goldstein Professorship at the Stanford University School of Medicine and serves as a professor in the Department of Molecular & Cellular Physiology, with appointments in the Departments of Neurology, Psychiatry, and Behavioral Sciences. During his nearly 20 years at Stanford, Prof. Südhof has focused his research on understanding and unraveling the mechanisms of synaptic transmission, synapse specification, and the link between synaptic genes and neuropsychiatric diseases.

In 2013, Thomas Südhof received the Nobel Prize in Physiology or Medicine for his work on the machinery that regulates vesicular trafficking, contributions that include elucidating how secretory vesicles dock, recognize calcium, and fuse. This award was shared with Randy W. Schekman and James E. Rothman. The jury recognized the fundamental impact of these pathways on intracellular transport and synaptic transmission. His Nobel Prize crystallized decades of presynaptic discoveries that today form the molecular basis of neuronal exocytosis.

One of the most significant anecdotes linked to the awarding of the Nobel Prize to Thomas C. Südhof in 2013, and which connects him in a very special way to our land, occurred precisely while he was driving to Baeza to participate in one of the scientific workshops organized by the International University of Andalusia, where he has participated on numerous occasions as an organizer and/or speaker.

Recognized by the Baeza City Council in 2017, his relationship with Spanish science dates back to the late 1990s, when he began a fruitful collaboration with the Department of Medical Physiology and Biophysics of the Faculty of Medicine of Seville. This relationship later expanded with the Institute of Biomedicine of Seville (IBiS), where he was honored in 2015 as an "IBiS Distinguished Investigator."

He has also served on the Scientific Advisory Board of the Cajal International Neuroscience Center (CINC) in Madrid, contributing to the development of neuroscientific research in Spain.

A profound admirer of the art and history of Andalusia and Spain, Thomas Südhof has taken advantage of each visit to discover and enjoy our heritage, stopping,

among other places, at the Jaén Cathedral, where he was impressed by the architecture of Andrés de Vandelvira.

Since winning the Nobel Prize, Südhof has maintained intense scientific activity at Stanford University, collaborated on consortia for modeling neurodegenerative diseases, such as projects related to Alzheimer's disease, and participated in advisory committees and biotechnology startups. In 2023, he was appointed to the Scientific Advisory Board of the Secretary-General of the United Nations (UN), reflecting his involvement in scientific advisory services at the highest levels. He also remains associated with the Howard Hughes Medical Institute (HHMI) and various international scientific academies.

Throughout his academic and professional journey, Thomas Südhof has embraced the famous phrase by Claude Bernard, considered the founder of experimental physiology: "The art of making discoveries consists in seeing what everyone sees and thinking what no one has thought."

As can be seen in the extensive and brilliant academic and research career of Professor Thomas Südhof, his constant pursuit of scientific excellence always stands

out. From the very beginning, he joined the laboratory of an excellent biochemist of the time, Professor Victor P. Whittaker, and later trained with researchers of the stature of Professors Michael S. Brown and Joseph L. Goldstein, who preceded him in winning the Nobel Prize and undoubtedly guided him in his pursuit and achievement of scientific excellence.

It is also important to highlight his commitment to multidisciplinarity, incorporating other fields such as biochemistry, physiology, molecular genetics, and structural biology, to name some of them, into the cellular and molecular foundations of neuronal synapses. Furthermore, throughout his scientific career, he has broadened his interest in science, beginning with chromaffin cells of the adrenal gland and later moving on to neuronal synapses, taking the basic mechanisms of their functioning as a reference in both cases. Once these essential pillars have been unraveled, he has gradually begun to seek their applicability, both for understanding pathophysiological processes and, from there, for the search for new therapeutic designs and targets.

His academic career is also an example of his commitment to science and scientific advancement, leading each of

his training stages with his commitment to management and institutional work to consistently develop a world-class academic unit.

Perhaps the awarding of the Nobel Prize in Medicine or Physiology is one of the most striking awards and distinctions at the social level, and with a global worldwide impact. However, it is important to highlight that Professor Thomas Südhof's list of achievements has been, and will surely continue to be in the future, filled with many other awards and distinctions. For example, in 1997 he received the United States National Academy of Sciences Prize in Molecular Biology, in 2004 the MetLife Prize for Alzheimer's Disease Research, and also in 2004 the Bristol-Myers Squibb Prize for Neuroscience Research. In 2010 he received the Kavli Prize in Neuroscience, jointly with James Rothman and Richard Scheller, and in 2013 the Lasker-DeBakey Prize in Basic Medicine, jointly with Richard Scheller, among many others prizes. Among his distinctions, it is worth highlighting the *Grande Médaille de la Ville de Paris*, together with James Rothman and Randy Schekman, in 2014, and the *Grosses Bundesverdienstkreuz mit Stern* (Grand Cross of Merit of the Federal Republic of Germany with Star) from the Federal Republic of Germany (*Bundesrepublik Deutschland*).

He is also an elected member of prestigious scientific societies, including the National Academies of Sciences, Medicine, Arts and Sciences of the United States of America, the Norwegian Academy of Sciences, the German Academy Leopoldina, and the Royal Society of London, among others.

Thomas Südhof has given countless invited lectures at the world's most prestigious scientific meetings, such as the Keystone and Gordon Conferences, to name a few, throughout his research career. Some years, his lectures were so numerous that he would barely have time to travel around the world to continue sharing his scientific findings. He has served on the editorial boards of numerous scientific journals, including *Neuron, the Journal of Biological Chemistry, Neuroscience*, the *Journal of Neuroscience*, and *Proceeding of the National Academy of Sciences U.S.A.*, among others. He has also co-founded several start-ups and serves on the scientific advisory boards of more than fifteen research centers and biotechnology/biomedical companies.

Finally, to give a comprehensive overview of Professor Thomas Südhof's excellence, a quick overview of his scientific output is reflected in his more than 700 published articles, many of which have been published

in the world's leading scientific journals such as *Cell, Nature*, and *Science*.

As can be seen in this brief summary of Thomas Südhof's academic, scientific, and professional career, his perseverance in the pursuit of scientific excellence has been one of his greatest achievements. I believe that having Thomas Südhof at the University of Jaén today is a privilege of which the entire university community should be very proud. I am also certain that his incorporation into our university's faculty should be a source of pride and inspiration for all the researchers who join us in this room today. Therefore, we must focus on their trajectory and follow the wise advice of Marie Curie, the first researcher to receive two Nobel Prizes, first in Physics (1903) and later in Chemistry (1911), who stated: "We should never stop until we have reached the highest point we can achieve."

Based on all the above, it is therefore unavoidable that Professor Thomas Sudhof is nominated as Doctor Honoris Causa by the University of Jaén at this solemn academic ceremony.