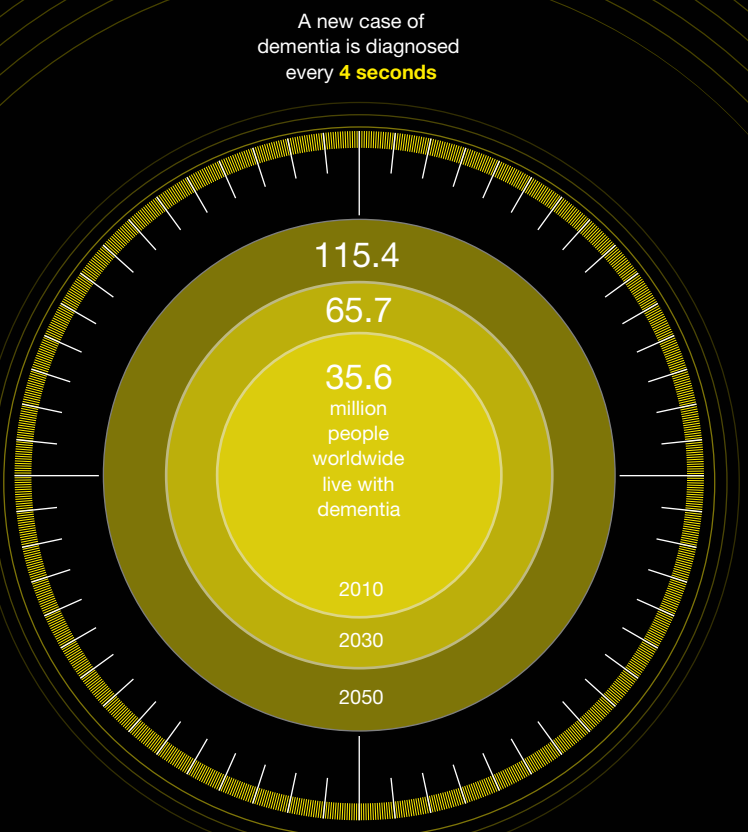


Dangerous **Mistaken Identity**

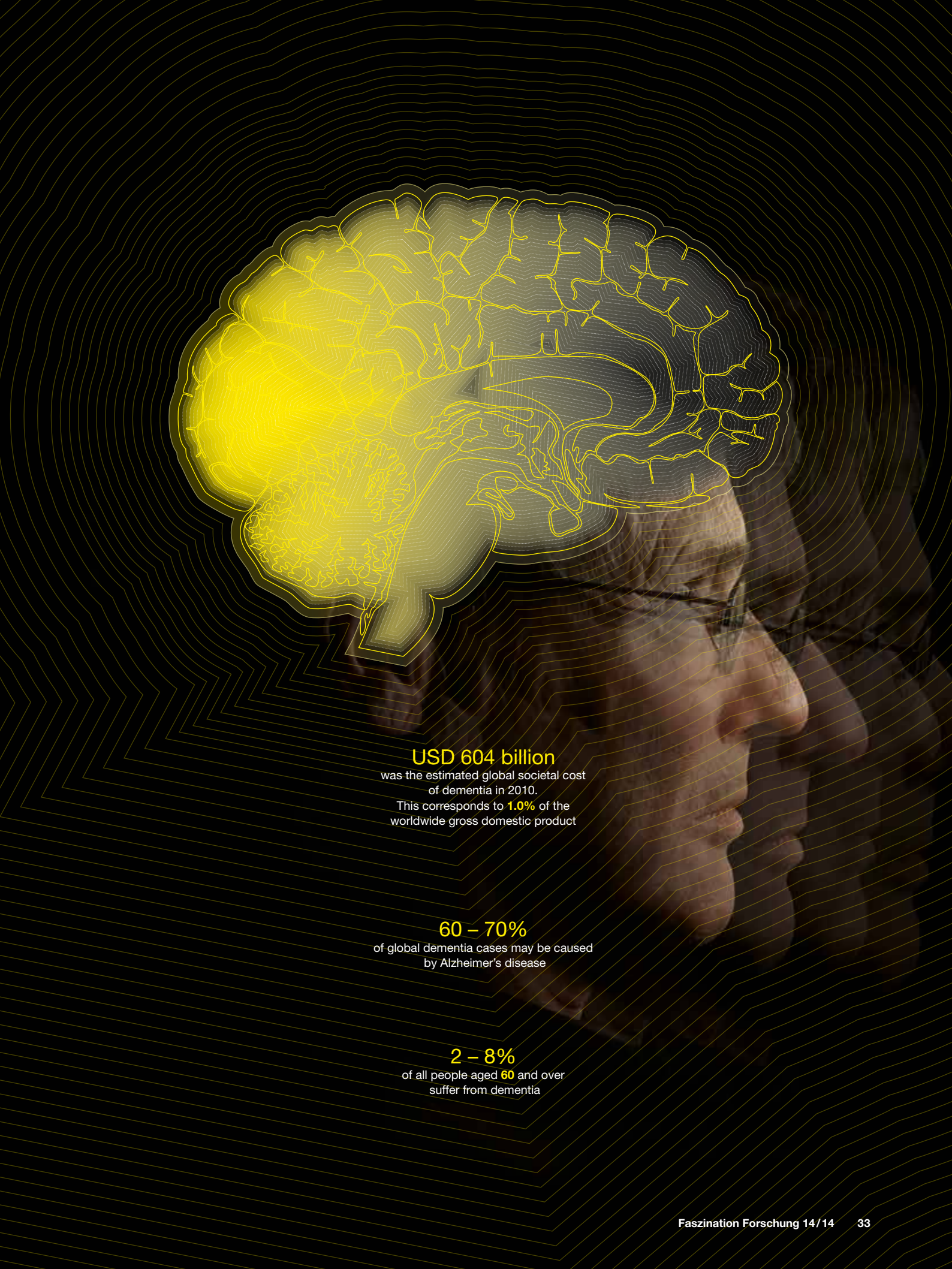
Chaperone binds protein responsible for Alzheimer's disease – scientists unveil the molecular recognition mechanisms behind the process

Link

www.madllab.ch.tum.de/

Tau proteins, which are responsible for Alzheimer's disease, bind to the folding protein Hsp90. The molecular recognition mechanisms that play a role here have been unveiled by an international team of scientists led by the Technische Universität München (TUM) and the Helmholtz Zentrum München (HMGU). This might open the door for new approaches for the treatment of Alzheimer's disease. Proteins like the so-called heat shock protein Hsp90 play an important role in almost all processes within human cells. They help other proteins fold into their three-dimensional structure or return damaged proteins back into their proper shape. Recently, there has been increasing evidence indicating that the heat shock protein Hsp90 may also be involved in the folding processes ▷

Graphics: edlundsepp (Source: WHO),
Picture credit: mammamaart (istockphoto.com)



USD 604 billion

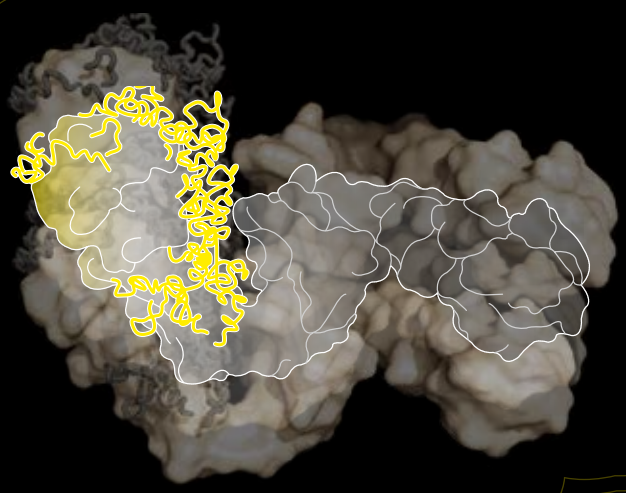
was the estimated global societal cost
of dementia in 2010.
This corresponds to **1.0%** of the
worldwide gross domestic product

60 – 70%

of global dementia cases may be caused
by Alzheimer's disease

2 – 8%

of all people aged **60** and over
suffer from dementia



Tau proteins, which are responsible for Alzheimer's disease, bind to the folding protein Hsp90. Scientists have now unveiled the structure and dynamics behind the interactions between the two biomolecules. The image shows a structural model of the Hsp90-tau protein complex aquired with magnetic resonance spectroscopy (NMR) and small-angle X-ray scattering (SAXS). (light grey: Hsp90; yellow: tau protein)

of the tau protein. Deposits of tau proteins in brain cells are typical for Alzheimer's disease and are held responsible for decaying nerve cells. However, while dissolved tau proteins look more like long, stretched chains, Hsp90 binds predominantly proteins that have already been prefolded. This contradiction has now been resolved by an international team headed by Dr. Tobias Madl, leader of the BioSysNet Working Group, TUM Junior Fellow and leader of the Emmy-Noether Group Structural Biology of Signal Transduction at the Institute of Structural Biology at the Helmholz Zentrum München, as well as Prof. Stefan Rüdiger from the Dutch University of Utrecht.

How the heat shock protein Hsp90 and the tau protein interact

Using a combination of very different techniques like magnetic resonance spectroscopy, small-angle X-ray scattering and computer modeling, they successfully determined structure and dynamics of the interactions between the two biomolecules: for Hsp90, the tau protein looks like a prefolded larger protein. Furthermore, they were able to deduce how Hsp90 influences the aggregation of tau proteins with one another.

"Deposits of tau proteins can cause Alzheimer's disease. We have discovered the protein regions in which the proteins interact. This is a novel and important starting point for influencing structural formation and for developing future therapies for Alzheimer's disease," says Madl. In addition to Alzheimer's disease, further neurodegenerative diseases are caused by protein aggregation. Chaperones also play a role in the development of cancer and cystic fibrosis. These scientific insights thus provide an important basis for better understanding the disease mechanisms. *Andreas Battenberg (TUM)*

Picture credit: Tobias Madl/TUM / HMGU

Der Moment, in dem Sie sicheren Boden betreten. Und begreifen, warum man bei uns immer wieder zu Höhenflügen starten kann.
Für diesen Moment arbeiten wir.

ZEISS ist ein weltweit führendes Unternehmen der Optik und Optoelektronik mit rund 24.000 Mitarbeitern. Zusammen mit den Besten ihres Fachs arbeiten Sie hier in einem kollegialen Klima für technologisch bahnbrechende Produkte. Mitarbeiter von ZEISS stehen leidenschaftlich dafür ein, immer wieder etwas zu schaffen, das die Welt ein bisschen besser macht.

Starten Sie Ihre Karriere bei uns: www.zeiss.de/karriere

ZEISS

We make it visible.