

Copy of the genetic makeup travels in a protein suitcase

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Scientists from the Institute for Physical and Theoretical Chemistry at the University of Bonn have succeeded for the first time in the real time filming of the transport of an important information carrier in biological cells that is practically unmodified. This paper has now been published in the highly regarded journal *Proceedings of the National Academy of Sciences*.

The blueprint of all living beings is stored in their genetic material. In higher <u>organisms</u> this is stored in the well-protected cell nucleus. "Here a kind of copier works around the clock to make copies of the information needed at the time," says first author Jan Peter Siebrasse from the Institute for Physical and <u>Theoretical Chemistry</u> at the University of Bonn. The copies contain the information which the cells need to produce vital enzymes or other cell <u>building materials</u>. These copies consist of messenger RNA which travels on random paths to the membrane of the cell nucleus and from there through the nuclear pores into the <u>cytoplasm</u> which fills out the cells like jello.

The working group has found out that the messenger RNA lingers briefly at the pores in the membrane of the nucleus before it is finally transported out – presumably for a final "quality control" or simply because it has to adjust in order to leave via the pore exit. The export process lasts in total only a few hundredths of a second to several seconds. "In all likelihood, the process needs much longer for larger, voluminous messenger RNA molecules than for smaller ones," adds Prof. Ulrich Kubitscheck, head of the working group Biophysical



Chemistry and senior author of the publication.

Interestingly enough, only about every fourth collision between arriving messenger RNA and the cell nucleus leads to a successful export. Here, two kinds of processes can be distinguished: On the one hand, brief collisions with the nuclear membrane where presumably no pore is hit, and, on the other hand, those transports that are slowly aborted perhaps on account of a deficient quality control.

The RNA is packed in a type of "suitcase" made of proteins for transporting. "And it is quite a chunk," grins Prof. Kubitscheck. This is why some of his colleagues presume there are helpers on the outside of the cell's nucleus which pull the "suitcase" through the pores, a theory which the professional physicist together with the molecular biologist Jan Peter Siebrasse are currently investigating

Just what exactly happens en route from the copier to the pores has been clarified in recent years among others by Prof. Kubitscheck's working group at the University of Bonn. "Key experiments on this were undertaken by the biologist Dr. Roman Veith, whose doctorate thesis was awarded this year's Dr. Edmund ter Meer Ph.D. thesis prize from the university society," reports Prof. Kubitscheck. For these experiments the messenger RNA was altered so that it glowed when illuminated with a laser beam. This enabled the researchers to trace the path of individual molecules containing copies of the genetic material in living buccal gland cells of a mosquito type with up to 500 pictures per second. A light microscope with a high speed camera made the observation possible.

Once the transport processes between the "copier" and the cell nuclear membrane were understood, Prof. Kubitscheck and his colleagues turned their attention in recent years to the direct transport process through the <u>nuclear pores</u>. In order to observe this process, they took a number of years to construct a highly sensitive light microscope which works on the



basis of target illumination. It creates delicate pictures of living samples and, in the process of taking pictures with high frequency, creates an unusually strong contrast.

The question of how the messenger RNA enters the cell from the <u>cell nucleus</u> is of fundamental interest in biology, a fact Prof. Thoru Pederson (University of Massachusetts Medical School) underscores in his comment which accompanies the article paper presented by the Bonnbased scientists. In recent years, there have been two publications on this performed by working groups in the USA and Israel. In these studies, however, the messenger RNA has been altered with additives making the molecules at least double their volume. By contrast, the Bonn-based working group modified the <u>messenger RNA</u> in a negligible way, as Prof. Pederson determined.

More information: Nuclear export of single native mRNA molecules observed by light sheet fluorescence microscopy, *Proceedings of the National Academy of Sciences* (PNAS), <u>DOI: 10.1073/pnas.1201781109</u>

Provided by University of Bonn

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