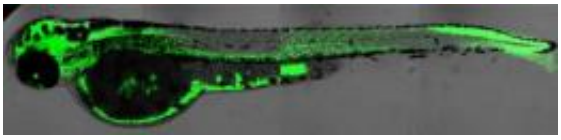
Visualization of DNA synthesis in vivo

December 13 2011



F-ara-Edu is injected into zebrafish eggs. Credit: University of Zurich

Researchers of the University of Zurich have discovered a new substance for labeling and visualization of DNA synthesis in whole animals. Applications for this technique include identifying the sites of virus infections and cancer growth, due to the abundance of DNA replication in these tissues. This approach should therefore lead to new strategies in drug development.

Interactions of biological macromolecules are the central bases of living systems. Biological macromolecules are synthesized in living cells by linking many small molecules together. Naturally occurring macromolecules include genetic materials (DNA) and proteins. A detailed understanding of the synthesis of these macromolecules in whole animals is a basic requirement for understanding biological systems, and for the development of new therapeutic strategies.

To visualize the synthesis of biomolecules in living organisms, artificial small molecules can be added to and incorporated by the cell's own biosynthetic machinery. Subsequently, the modified biomolecules containing the artificial units can be selectively labelled with fluorescent

substances. Until now, this approach had one major limitation: the substances used for labelling were toxic and caused cell death.

Anne Neef, a PhD student from the Institute of Organic Chemistry at the University of Zurich, has developed a new substance that can replace the natural nucleoside thymidine in DNA biosynthesis. This fluorinated nucleoside called "F-ara-Edu" labels DNA with little or no impact on genome function in living cells and even whole animals.

"F-ara-Edu" is less toxic than previously reported compounds used for DNA labelling and it can be detected with greater sensitivity. "F-ara-Edu" is therefore ideally suited for experiments aimed at "birth dating" DNA synthesis in vivo. "As a demonstration of this, F-ara-Edu was injected into Zebrafish eggs immediately after fertilization. Following development and hatching of the fish, the very first cells undergoing differentiation in embryonic development could be identified", explains Anne's research advisor, Prof. Nathan Luedtke.

"By visualizing new DNA synthesis in whole animals, the sites of virus infection and cancerous growth can be identified due to the abundance of DNA replication in these tissues", adds Prof. Luedtke. This approach should therefore lead to new strategies in drug development.

More information: Anne Brigitte Neef, Nathan William Luedtke. Dynamic metabolic labeling of DNA in vivo with arabinosyl nucleosides. *Proceedings of the National Academy of Sciences. PNAS.* November 29, 2011. doi:10.1073/pnas.1101126108

Provided by University of Zurich

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