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Novel chemistry-based tools to study epigenetic enzymes in inflammation

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Chronic inflammatory diseases, such as, for example, asthma, afflict millions of people worldwide. In such diseases enzymes are crucial regulators and therefore represent potential drug targets. Nevertheless, the activities of these enzymes are poorly studied due to a lack of convenient tools for modulation and detection. To address this problem further, we are developing novel detection methods and small molecule inhibitors to study signal transduction pathways that are involved in inflammation. Our studies focus on protein acetylations at lysine residues, which have a versatile regulatory role in signal transduction pathways. Among others lysine acetylations, are key regulators of the histone code in epigenetic regulation of gene transcription. We are developing a novel strategy to study protein acylation using metabolic labelling with alkenylated short fatty acids, which can be detected by bioorthogonal ligation of detection labels using the oxidative Heck reaction. This strategy enables the identification of novel protein acylations sites. The novel ligation method proved to be a robust replacement for the frequently used alkyne labelling in combination with the 'click reaction'. In addition, mass spectrometry analysis was utilized to quantify endogenous protein lysine acetylations. Interestingly, this method also enabled the identification of cross-talk of lysine acetylation with other posttranslational modifications in signal transduction pathways.

Biography

Frank J Dekker has completed his PhD at the age of 26 years from Utrecht University, The Netherlands, and he did postdoctoral studies at the Max-Planck Institute for molecular physiology in Dortmund, Germany. He is now an Associate Professor in Chemical Biology at the University of Groningen, The Netherlands. He has published more than 40 papers in reputed journals and received prestigious research grants from national funding agencies and the European research council (ERC).

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