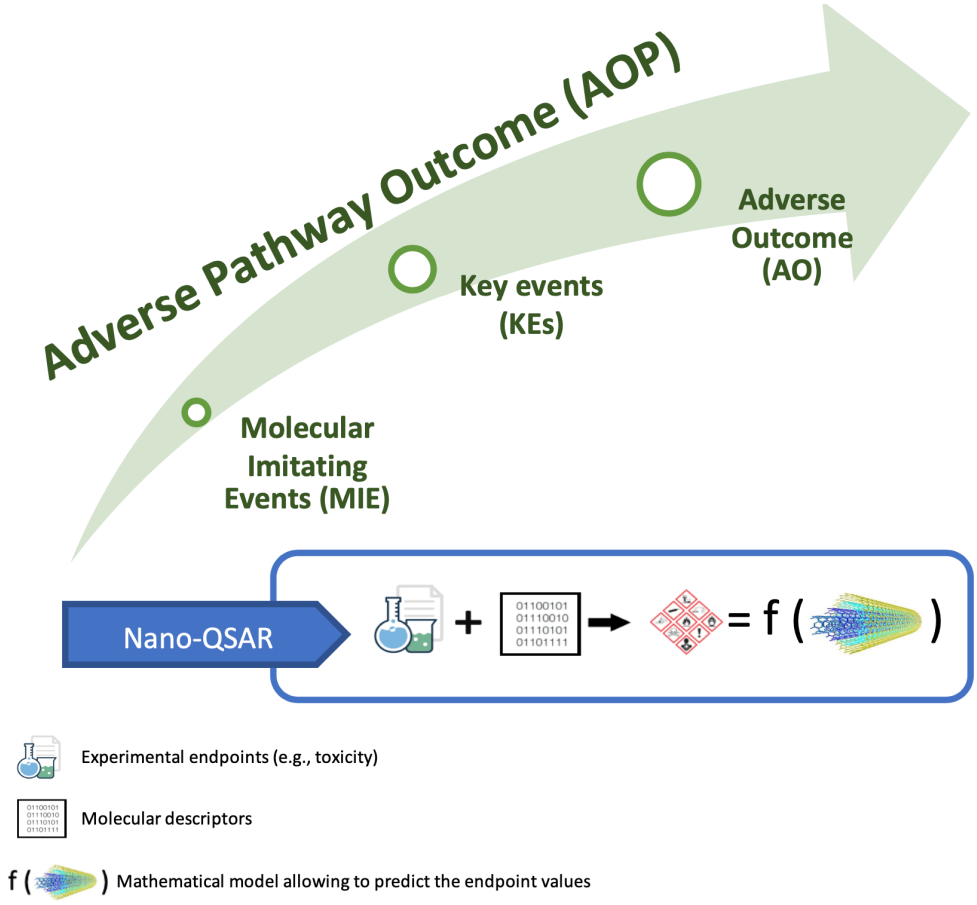
AOP to support the use of QSAR models

Background

Adverse Outcome Pathway (AOP) is a simplified depiction of complex toxicological processes in a linear and modular format. AOP describes a mechanism underlying a toxicological response that is initiated by the occurrence of a biological event after substance exposure. The so-called molecular initiating events (MIE) initiate a series of intermediated key events (KEs) which lead to an adverse outcome (AO).

The AOP framework follows the philosophy of developing novel, alternative methods to animal testing and aimed at understanding the mode of actions leading to an AO. In line with this strategy, there are also the Quantitative Structure Activity Relationships (QSAR) models, which allow the identification of the key structure-related-properties crucial for the events leading to an AO. PATROLS aimed to verify the hypothesis that AOPs can support Nano-QSAR model development.



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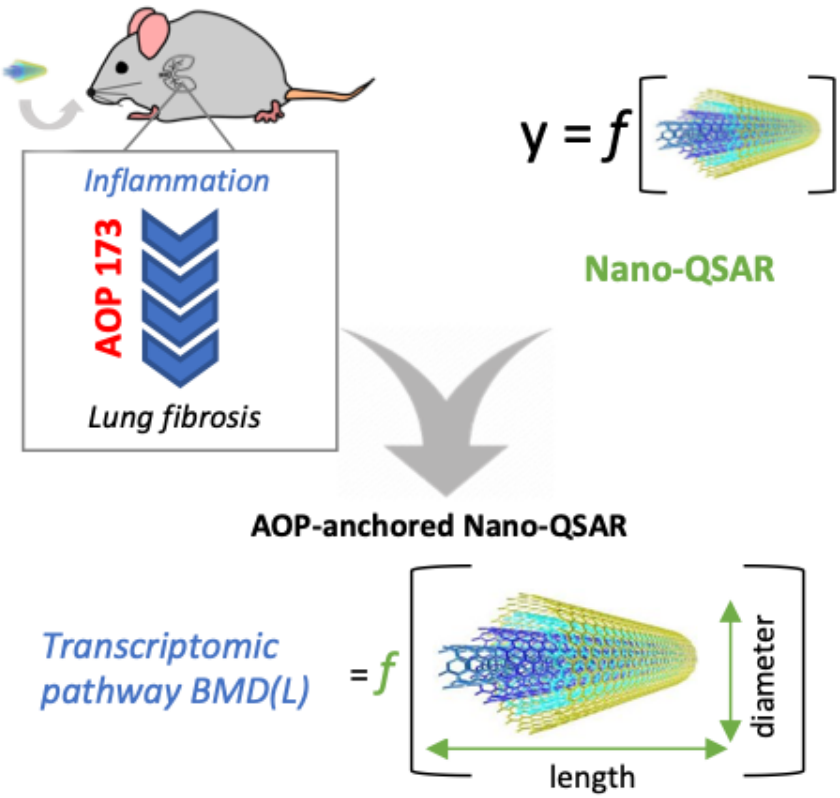
Outcomes

Within PATROLS the transcriptomic-based and AOP-anchored Nano-QSAR model was developed. The AOP173 was applied, and the model designed to predict pulmonary pathology induced by multiwalled carbon nanotubes (MWCNTs) was delivered. This model quantified the influence of the structural properties of MWCNTs upon lung tissue inflammatory responses observed at the transcriptomics level. Using the aspect ratio of MWCNTs as a predictor, one can predict the biological event that initiates the inflammation process described by the 'Agranulocyte adhesion and diapedesis' pathway. In effect, the mechanism of pulmonary pathology induced by MWCNTs was determined. Thus, the concept of combining the AOP with the Nano-QSAR may support the better understanding the adverse effect of nanomaterials on human health and form the basis for comprehensive and realistic risk assessment.



This factsheet is based on the publication: Jagiello, K., Halappanavar, S., Rybińska-Fryca, A., Williams, A., Vogel,U., Puzyn, T.: Transcriptomics-based and AOP-informed structure-activity relationships to predict pulmonary pathology induced by multiwalled carbon nanotubes" Small, Doi: 10.1002/smll.202003465

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