

**Synthetic Molecular Motor Activates Drug Delivery from Polymersomes**

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The development of stimuli-responsive, smart delivery systems in nanomedicine arises from the limitations, side effects and unsolved needs of current drug delivery. [1] In our study, we developed a highly spatiotemporal controlled delivery system with tunable release profile. [2] A hydrophobic synthetic molecular rotary motor is embedded in the hydrophobic domain of a PDMS-*b*-PMOXA diblock copolymer, resulting in a responsive self-assembled system. The release of a fluorescent dye with high efficiencies is triggered by the successful incorporation of the motor and its selective activation by low energy visible light ( $\lambda = 430$  nm, 6.9 mW). Moreover, the system presents a responsive behavior due to its ability to turn on and off on demand over sequential cycles and even low concentrations of the photo-responsive unit are shown to effectively promote release. Our system was further investigated under relevant physiological conditions, encapsulating the FDA approved drug, Pemetrexed and tested on a lung cancer cell line. When compared to free given drug, similar levels of cell viability are observed, highlighting the potential of our platform to deliver functional drugs on request with high efficiency. This work is an important step in the field of next generation smart delivery systems exploiting the application of synthetic molecular machines.

[1] Simona Mura, Julien Nicolas & Patrick Couvreur, *Nature materials*, **2013**, 12, 991-1003.

[2] Ainoa Guinart, Maria Korphidou, Daniel Doellerer, Gianni Pacella, Marc C. A. Stuart, Ionel Adrian Dinu, Giuseppe Portale, Cornelia Palivan, Ben L. Feringa, *PNAS*, **2023**, in press