Multi-chromatic control of mammalian gene expression and signaling

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Processes in multicellular systems are orchestrated by gene expression programs that are tightly regulated in time and space and many biological processes require the coordinated activation of several genes. The targeted manipulation of such processes by synthetic tools with high spatiotemporal resolution could, therefore, open new opportunities in tissue engineering and enable a deepened understanding of developmental processes.

We have developed the first red/far-red light-triggered gene switch as well as an ultraviolet B (UVB)-inducible expression system for mammalian cells to achieve gene expression control in time and space. To set-up the red/far-red light-triggered gene switch, we capitalized on the red light-dependent interaction of the *A. thaliana* proteins phytochrome B (PhyB) and the phytochrome interacting factor 6 (PIF6). This design resulted in a switch that can be toggled between stable on- and off-states using short light pulses at 660 or 740 nm. The UVB-responsive split transcription factor is based on the *A. thaliana* UVB receptor UVR8 and the WD40 domain of COP1. By combining this UVB-responsive system with the PhyB-based red light-inducible gene expression system and blue light-inducible gene control technology, we demonstrate multi-chromatic multi-gene control by differentially expressing three genes in a single cell culture in mammalian cells. Furthermore, we apply this system for the multi-chromatic control of angiogenic signaling processes.

We expect that this multi-chromatic approach for the control of gene expression will enable unprecedented spatiotemporally controlled molecular interventions in cells, tissues and organisms.