

## **Towards Artificial Spores: Chemical Reactions on the Interface of Living Cells**

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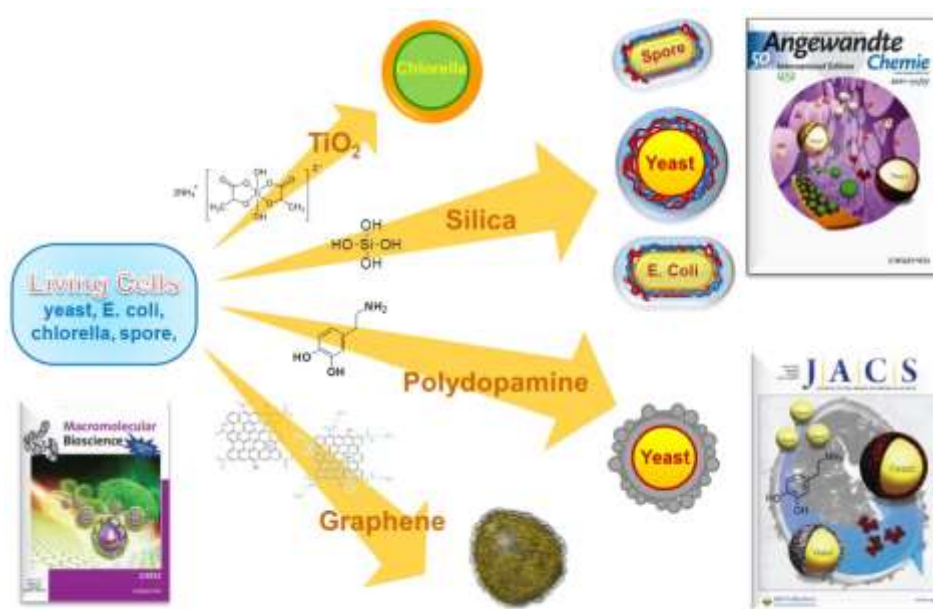
### **Extended Abstract**

Nature has found cryptobiotic ways to preserve genetic information and protect cellular components against external stresses, such as nutrient deprivation, desiccation, high temperatures, radiation, and caustic chemicals (Keilin, 1959). For example, a bacterial endospore, usually formed in response to nutrient deficiency, is a non-dividing, dormant body, which possesses a thin but tough proteinaceous coat at its outmost layer. Beneath the coat is a buffering cortex layer of peptidoglycan. This hierarchical shell structure allows the endospore to survive for many years (in some cases, up to millions of years) under hostile conditions found naturally that can easily and quickly kill normal cells.

In natural endospores, preservation is mainly achieved by the physicochemical robustness of the outer organic shells. It has, however, been practically difficult to achieve biochemical compatibility of living cells with robust artificial shells, as the synthesis of robust materials generally requires harsh conditions that interfere with the viability of the cells. In this respect, the essential step for the formation of strong artificial shells is to develop bio- and cytocompatible materials and synthesis reactions. Over the past decade, researchers have attempted to ‘coat’ living cells with various macromolecules (Fakhrullin et al., 2012). Although the macromolecule-based coatings are cytocompatible and the method of cell coating is effective, the coatings are not sufficiently robust to physicochemically protect living cells. Recently, several strategies have been suggested to provide robust artificial shells to encapsulate living cells, thereby forming artificial spores. Newly-developed strategies are based on the chemical reactions occurring on the interface of living cells, which include: cross-linking of polymeric films, bioinspired mineralization, and mussel-inspired polymerization (Yang et al., 2013; Yang et al., 2012a; Yang et al., 2011a; Yang et al., 2009; Yang et al., 2012b; Yang et al., 2011b).

Recent studies have sought to chemically control and tailor the metabolic behaviours of non-spore-forming cells, as well as enhancing their viability against adverse environmental conditions, by forming thin (<100 nm), tough artificial shells. These living ‘cell-in-shell’ structures, called artificial spores (chemically-formed spore-like structures), enable control of cell division, protection against physical and chemical stresses, and cell-surface functionalizability, as well as providing the cells with exogenous properties that are not innate to the cells but are introduced chemically, such as magnetism, heat-tolerance, and UV-resistance. The physicochemical durability and biological stability of spores would be beneficial for the realization of cell-based sensors, cell therapy, regenerative medicine, as well as for fundamental studies on cellular metabolism at the single-cell level and cell-to-cell communications (Hong et al., 2013).

This presentation focuses on chemical approaches to single-cell encapsulation with artificial shells for creating artificial spores, including cross-linked layer-by-layer assembly, bioinspired mineralization, and mussel-inspired polymerization. Various reported approaches to shell formation are reviewed herein, including a review of the properties of the formed shell. The current status and future prospects of this emerging field are also discussed.



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