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Nanomaterial Interfaces in Biology

Methods and Protocols

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Preface

The intersection of nanotechnology with biology has given rise to numerous ideas for new ways to use nanotechnology for biological applications. Nanomaterials possess unique size- and material-dependent properties, which make them attractive for improving regular biomedical fields, such as drug delivery, imaging, therapy, and diagnostics as well as next-level developments, comprising activation/deactivation, mimicking, and implementation of biomolecular systems and functions. Consequently nanotechnology has held great potential for novel and unique capabilities, and stirred the imagination of many scientists.

While nanotechnology and nanoscience has held great promise for revolutionizing biology, it has been hindered by the fact that when nanomaterials are interfaced to biomolecules or put into biological environments, many undesirable side effects result, such as aggregation and nonspecific adsorption, which can compromise biological function or give rise to negative biological responses. This can be largely attributed to a range of interface and intermolecular interactions between the nanomaterials with the biomolecules as well as the solvent that mediates their interactions. These interactions are difficult to control, predict, and prevent. Interface effects of inorganic surfaces have been a major issue historically, manifesting as surface fouling of medical device implants and stents. Unfortunately, these effects worsen or give rise to new and unexpected complications for nanoscale materials because surface volume ratios are exponentially higher, and nanoscale surfaces have different physical and chemical properties.

Therefore, despite the fact that we now have a high degree of control over the synthetic properties of the nanomaterials, similar control over their interfaces to biology has yet to be achieved. This is crucial as their biological interface ultimately determines their biological identity and fate. In the last 10 years, the biological–nanomaterial interface has created unprecedented challenges not only for finding useful ways to exploit nanomaterials in biology but also in their unintentional consequences, such as environmental and toxicological effects. For example surface fouling, nonspecific adsorption, or unexpected aggregation and instability have prevented many of the exciting and early ideas of nanobiotechnology from reaching fruition.

We believe a key pitfall that plagues this area is the difficulty in reproducing results, where a huge amount of variability exists not only between different labs but also from day to day in the same lab. This variability is almost never reported in peer-reviewed journal papers, despite its criticality. Also, members of the nanotechnology community typically come from chemistry, physics, and materials science, and historically are not accustomed to providing stepwise protocols. Therefore, a handbook of detailed protocols and best practices for this field is critically needed.

While there have been some examples of individual protocols in protocol literature such as *Nature Methods*, *Current Protocols*, *Molecular Cloning*, and on the National Cancer Institute's Nanotechnology Characterization Laboratory website, we believe that it is time to provide a consolidated volume of step-by-step protocols in the tradition of *Methods in Molecular Biology*. *Methods in Molecular Biology* has played a major role in providing biological recipes and protocols, and in doing so has advanced biology in immeasurable ways. By creating standards for everyone and making experimental techniques more accessible, *Methods in Molecular Biology* has accelerated the discovery process. What used to be difficult experimentally now can be done by nearly anyone. These new tools have benefited the entire biology community, enabling huge leaps and bounds in scientific discovery and applications.

Thus, we present this volume with the hopes of improving the utility of nanotechnology as a tool to advance biological and medical sciences. While this volume is far from comprehensive, we hope that it will serve the new and emerging community well, and enable new capabilities and technologies that were not previously possible. The proposed protocols predominantly deal with nanomaterials, covering many of the now classic subjects, such as conjugation of nanoparticles to biomolecules and their applications in drug delivery or imaging. Additionally, some chapters are dedicated to flat surfaces because most of the methods for manipulating nanomaterials stem from those of flat surfaces, facilitated by fabrication advances to shrink the dimensions of materials.

The volume is organized into three parts: (1) protocols describing synthesis, fabrication, and construction of bio-nanomaterial interfaces, (2) characterization protocols of bio-nanomaterial interfaces, and (3) applications which utilize the bio-nanomaterial interfaces. We would like to note that we are not including significant coverage of toxicology and the unintended effects of nanomaterials. Due to the evolving scope of the toxicological studies of nanomaterials, the current state of the art is still developing, and thus is difficult to cover adequately in this volume of *Methods in Molecular Biology*. However, we hope that this collection will aid this growing field by serving as a guide.

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