Scalable Nanomanufacturing of Cyclic Peptide-based Nanorobots for *In Vivo* Sensing

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The development of a scalable nanomanufacturing platform to fabricate cyclic peptide-based nanorobots for biomedical applications, such as *in vivo* sensing, disease diagnosis, and targeted drug delivery is described in **Fig. 1**. The primary goal of this research is to determine the fundamental engineering principles related to scalable nanomanufacturing of self-assembled bio-molecules. The principles learned through this research will be applicable to various nanomanufacturing processes with self-assembly as a key step for bottom-up manufacturing. Upon development and optimization for the fabrication process, the medical community will benefit from the nanorobots for nanomedicine. Several important achievements have been made through our research supported by this NSF grant. ***Fist***, a new PEG-modified DOX-loaded cyclic peptide based nanotube (CPN) used for cancer therapy has been developed. Compared to free DOX, the PEG-modified DOX-loaded CPNs demonstrated higher cytotoxicity, increased DOX uptake and altered intracellular distribution of DOX in human breast cancer MCF-7/ADR cells *in vitro*. In addition, an enhanced inhibition of P-gp activity shows their potential to overcome the multidrug resistance in tumor therapy [1]. ***Second***, we have designed and fabricated the tunable self-assembled CPNs through investigating and optimizing multiple parameters including the length and density of PEG, cyclic peptide sequence and concentration, self-assembly and purification methods. The resulted scalable nanomanufacturing platform leads to a tunable synthesis of CPNs with desired physical and chemical properties [2]. ***Finally***, the tunable cyclic peptide nanotubes as visible fluorescent biomarkers for *in vivo* sensing have been developed and characterized. It will overcome many limitations of current green fluorescent proteins (GFPs). Based on the study, we currently are fabricating and validating a stimulus-responsive hybrid nanorobot with controllable sizes using CPNs and DNA aptamers for *in vivo* sensing and disease diagnosis, and further investigating the tunable cyclic peptide nanotubes as visible fluorescent biomarkers for *in vivo* sensing.

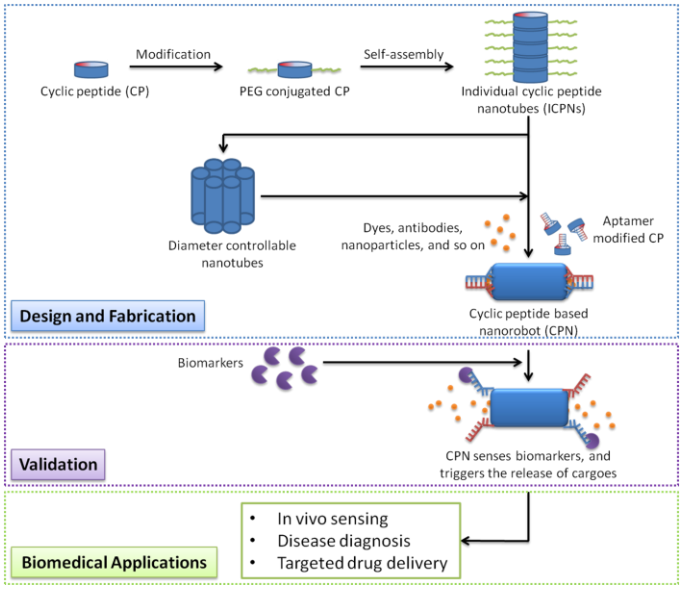

Fig. 1 Overview of the design, fabrication, validation and biomedical applications of the cyclic peptide nanotubes based nanorobots.

References

[1] Wang Y, Yi S, Sun L, Huang Y, Lenaghan SC, Zhang M. Doxorubicin-Loaded Cyclic Peptide Nanotube Bundle Overcome Chemoresistance in Breast Cancer Cells. Journal of Biomedical Nanotechnology. 2014;10:445-54.

[2] Leming Sun, Yongzhong Wang, Yujian Huang, Mingjun Zhang. Self-assembly of Individual Cyclic Peptide Nanotubes (ICPNs) for *In Vivo* Sensing. BMES 2014 Annual Meeting. October 22-25, 2014, San Antonio, Texas.