Weill Cornell Medicine

Engineered C' Dots Restore Tumor Microenvironment Homeostasis to Enable Effective Cancer Immunotherapy

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Background & Unmet Need

- Immune suppressive tumor microenvironments (TME) are a major barrier to effective cancer therapies, particularly in relapsed and refractory solid tumors (e.g., ovarian, breast, lung, and endometrial cancers)
- Current immunotherapies, including CAR T cell therapies, face significant challenges due to limited immune cell activation and tumor heterogeneity
- FDA-approved cytotoxic and immunotherapy treatments fail to control tumor growth in 'cold' TMEs due to complex immunosuppressive networks, metabolic dysregulation, impaired immune cell infiltration, and pro-tumoral inflammation
- **Unmet Need:** Therapeutic strategies capable of simultaneously reprogramming the immunosuppressive TME, restoring anti-tumor immunity, and re-establishing homeostasis to enable durable treatment responses

Technology Overview

- **The Technology:** A method for treating cancer by combining systemically deliverable immunomodulatory nanoparticle conjugates
- The nanoparticle conjugates are ultrasmall (<20 nm) silica-based nanoparticles
- **PoC Data:** The nanoparticles suppress TAMs and MDSCs while increasing CD8+/Treg ratios by >100x in mouse ovarian cancer models
- Enhanced tumor-cell uptake through anti-MUC16 targeting scFv-conjugated particles, resulting in ~10x greater uptake than non-targeted equivalents
- Demonstrates ferroptosis-dependent tumor cell death, synergizing with CAR T therapies to achieve a >70% reduction in tumor volumes in preclinical studies

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Gabriel DeLeon
Barney Yoo

Patents:
US Application Filed

Publications:
De Leon et al. *Nature Nanotechnology*. 2025

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TAM: tumor-associated macrophages
MDSC: myeloid-derived suppressor cells

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Technology Applications

- Synergistic treatment with cell therapies to enhance immune response and overcome tumor microenvironment suppression
- Standalone therapeutic platform to boost anti-tumor immunity and target cancer cells directly
- Dual theranostic capabilities integrating real-time tumor imaging with synergistic therapeutic delivery

Technology Advantages

- Provides intrinsic therapeutic effects and targeted drug/radiotherapeutic delivery
- Systemically deliverable for superior biodistribution, tumor penetration, and renal clearance
- Enables optimized combination therapies for heterogeneous tumor microenvironments.

Supporting Data / Figures

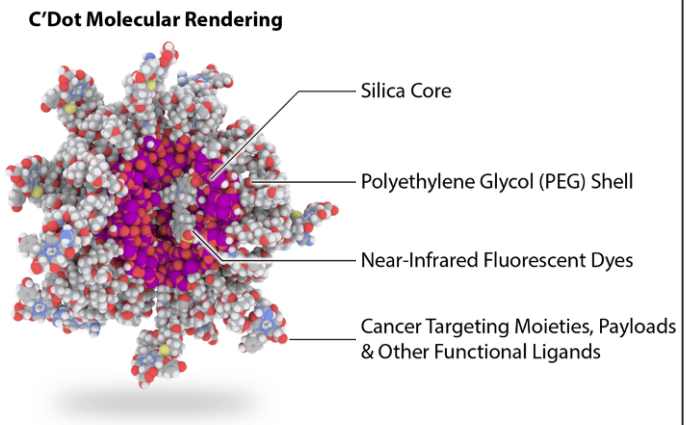

Figure 1: C-Dots are constructed with a three-dimensional (3D) crosslinked silica network core, which serves as a platform for the covalent attachment of biocompatible polymers, functional peptides, drugs, and contrast agents.

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