

Technology Snapshot

Technology Licensing Opportunity

TIDAL: Target-Induced Droplet Assembly of Ligands

Value Proposition

Developed by Los Alamos National Laboratory, TIDAL transforms the small antibody fragments known as nanobodies into a programmable, protein-only material that organizes itself on demand. By harnessing a natural process called liquid-liquid phase separation, TIDAL lets these binders gather into dense, dynamic droplets precisely when they encounter their intended target, giving developers a single platform that can purify proteins without costly resins, deliver drugs as a self-forming slow-release depot and even trap harmful proteins inside living cells. The outcome is a versatile toolkit that lowers production costs, simplifies manufacturing and opens fresh therapeutic and diagnostic possibilities, all from a building block that biology already knows how to make.

Technology Readiness Level 3

IP Information

S-197478, U.S. Patent pending

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Overview

At the heart of TIDAL is a small, engineered tag, called an encapsulation peptide (EP), that is fused to a nanobody. When many of these tagged nanobodies are present, they undergo liquid-liquid



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phase separation, similar to what makes oil bead up in water, and they collect into concentrated liquid droplets made entirely of protein. Binding to the target molecule intensifies the effect, so the droplets form most strongly exactly where and when that target is present. Because the assembly is dynamic and reversible, the droplets behave as stimuli-responsive materials whose thickness and flow can be tuned by the target ligand, allowing one design to serve as a purification handle, a delivery vehicle or an intracellular trap.

Advantages

- Cuts protein purification costs by replacing slow, expensive column resins with a simple trigger-and-precipitate step
- Enables patient-friendly, at-home injections that stay liquid in the syringe then set into a slow-release depot
- Works entirely from protein, avoiding synthetic carriers and easing manufacturing
- Can operate inside living cells to trap and neutralize harmful proteins linked to cancer or viral infection
- Boosts diagnostic sensitivity by concentrating faint signals into detectable droplets
- Offers one adaptable platform spanning manufacturing, therapy and detection

Continued on reverse

Technology Description

TIDAL: Target-Induced Droplet Assembly of Ligands treats the nanobody itself as a structural component rather than merely a binding reagent. Each fusion polypeptide pairs a target-specific nanobody with the encapsulation peptide (EP), and it is the peptide that drives the many weak, cooperative interactions responsible for phase separation. In solution these interactions produce biomolecular condensates, dense droplet phases that concentrate the nanobodies far above their ordinary levels; the presence of the matching ligand pushes the balance further toward condensation. Because condensation is governed by many cooperative contacts rather than a single rigid bond, the droplets stay liquid-like and dynamic, and their formation can be reversed when the trigger is removed.

Building on that behavior, the droplets function as programmable modules for delivery, stability or signal enhancement. Their rheology, meaning how readily they flow, can be switched by the target ligand, so a preparation can remain fluid enough to pass through a fine needle yet convert into a slow-release depot once injected. The same concentrating power lets the droplets scavenge and enrich internalized components to levels far above normal, which sharpens detection in diagnostics, and, when produced inside cells, the condensates can sequester disease-driving proteins such as oncogenic or viral factors into synthetic granules that block their activity. Purification follows the same logic: Triggering condensation precipitates the bound target out of solution, offering a resin-free alternative to the slow and expensive column methods used today.

Market Applications

- **Biopharmaceutical Manufacturing** (antibody and enzyme purification, protein production)
- **Therapeutics and Drug Delivery** (subcutaneous slow-release treatments, intracellular protein targeting)
- **Diagnostics** (high-sensitivity detection assays, point-of-care testing)
- **Biotechnology** (resin-free enzyme immobilization, biocatalysis)
- **Reagents** (protein capture, condensate-based cell studies)