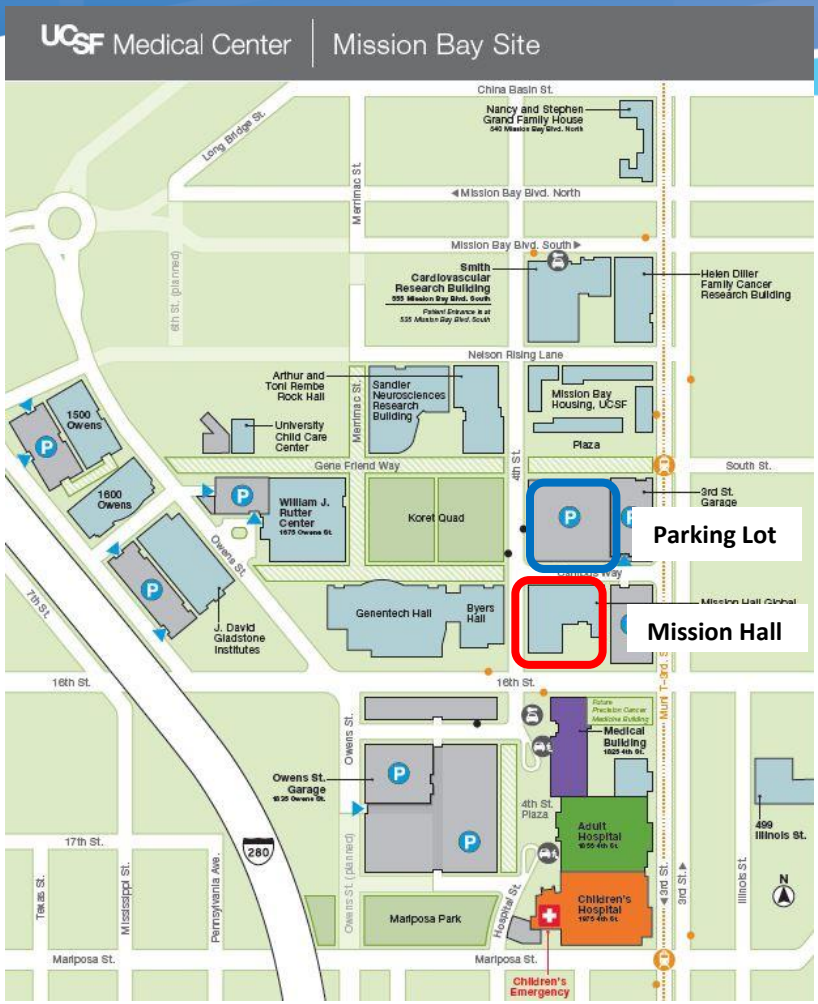
KOLIS 2017

KOLIS

2017 Spring Conference at UCSF Mission Hall Conference Room 1400

May 6th, 2017

KOLIS



Children's Emergency

Muni Bus Stop
UCSF at Mission Bay is accessible via Muni bus routes 22–Fillmore, 55–16th Street, and 91–Owl. All listed routes are accessible via wheelchair.

Muni T–3rd St. Light Rail
Muni streetcar line, T–3rd St. stops at 3rd St. and South St. as well as 3rd St. and Mariposa St. This route is accessible via wheelchair. For more information, visit sfmta.com.

Parking Entrance

Patient Drop–Off
Patients may be dropped–off at the circle drives in front of the Hospitals and in front of the Medical Building.

Public Parking
See map to the left for public parking locations. Primary access to the Owens St. Parking Garage is on Owens St.

UCSF Shuttle Stop

Valet Parking
Medical Building: Service is available Monday to Friday from 8:00 a.m. to 6:00 p.m. Vehicle drop–off is until 3:00 p.m. and valet vehicle retrieval until 6:00 p.m. After hours, vehicle keys will be available with a UCSF parking attendant.

Smith Cardiovascular Research Building: Service is available Monday to Friday from 7:30 a.m. to 3:45 p.m.

UCSF Mission Hall: https://goo.gl/maps/vj9uu9z16xm

550 16th St, San Francisco, CA 94158

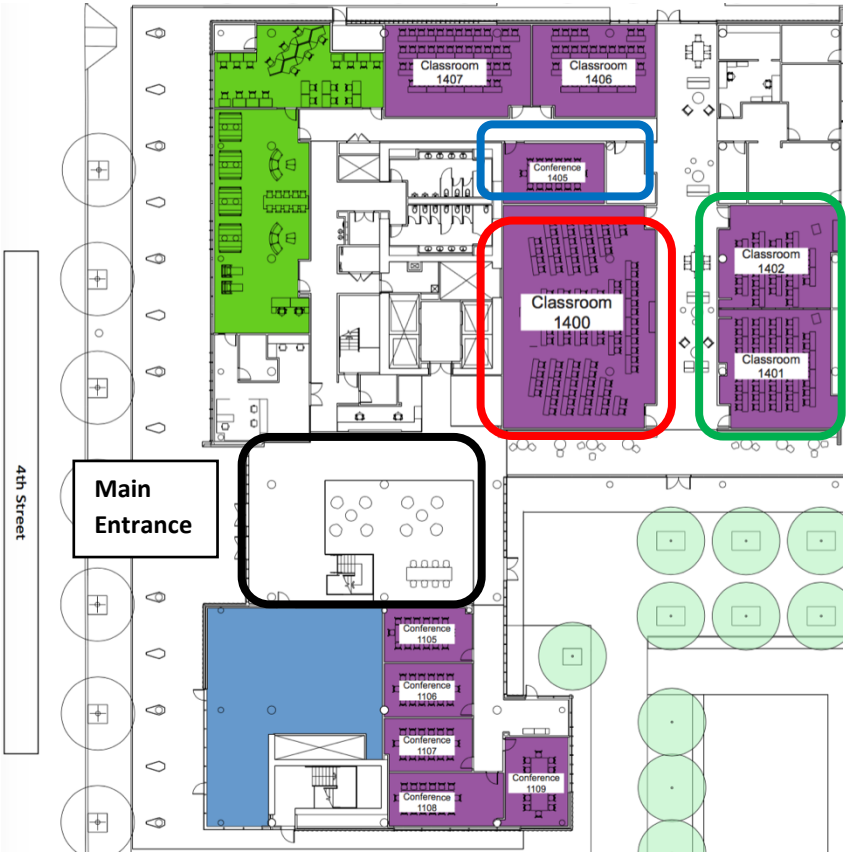
Surface Lot: https://goo.gl/maps/7YMo2s5iFEq

Main Lobby - Registration

1400 – Main Conference Room

1401&1402 – Extra Rooms

1405 – Daycare and Rest Area



PROGRAM

9:50-10:20 AM	**Registration** *Lobby, UCSF Mission Hall*
10:20-10:30 AM	**Opening Remarks** *Hyun Yong Jin, Ph.D., KOLIS President*
	Keynote Talks
10:30-11:10 AM	**Youngho Seo, Ph.D.** *Associate Professor at UCSF*
11:10-11:50 AM	**Seung Wuk Lee, Ph.D.** *Professor at UC Berkeley*
11:50-12:30 PM	**Sung Jin Kim, Ph.D.** *Associate Professor at UC Davis*
12:30-1:20 PM	**Photo Shoot and Lunch**
	Special Session #1
1:20-1:40 PM	**Jae-Hak Kim, Esq.** *Managing Partner, Doeul Law LLP (info@doeullaw.com)*
	Research Talks #1
1:40-2:00 PM	**Joonseok Cho, Ph.D.** *Postdoctoral Associate at Stanford University*
2:00-2:20 PM	**Hee Jeung Oh, Ph.D.** *Postdoctoral Associate at UC Berkeley*
2:20-2:40 PM	**Siyeon Rhee, Ph.D.** *Postdoctoral Associate at Stanford University*
2:40-3:00 PM	**Jae Ho Sohn M.D., M.S.** *Resident Physician at UCSF*

PROGRAM

3:00-3:20 PM — **Coffee break**

Special Session #2

3:20-3:40 PM — **Biosimilar Development at Samsung Bioepis**
Paul H. Song, Vice President of Samsung Bioepis (hys.song@samsung.com)

Research Talks #2

3:40-4:00 PM — **Hee Won Yang, Ph.D.**
Postdoctoral Associate at Stanford University

4:00-4:20 PM — **Joon Yong An, Ph.D.**
Postdoctoral Associate at UCSF

4:20-4:40 PM — **Taehong Yang, Ph.D.**
Postdoctoral Associate at Stanford University

4:40-5:00 PM — **Hee Jung Yang, Ph.D.**
Postdoctoral Associate at UC Davis

5:00-5:20 PM — **Seung-min Park, Ph.D.**
Instructor at Stanford University

Closing Remarks and Raffle

5:20-5:40 PM — **Closing**
Kyung Duk Koh, Ph.D., KOLIS Vice President

Raffle
Ara Hwang, Ph.D., KOLIS Treasurer
and
Jonghoon John Chang, KOLIS Planning Manager

5:40-6:40 PM — **Dinner and Networking**

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KEYNOTE TALKS

Plenary Talk 1 **Time: 10:30-11:10 AM**

How low is really low? Can we do even more with not many photons?

Youngho Seo, Ph.D.
Associate Professor at UCSF
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When patients are undergoing medical treatment, depending on the cases, they also go through many radiologic imaging studies to monitor the progress and determine the best course of actions. In these radiologic imaging studies, for serious disease implications such as cancers, cardiovascular diseases, and neurological disorders, CT, MRI, and PET are commonly used. Radiation exposure from ionizing radiation used in CT and PET is often inevitable. Although radiation exposure is fully justifiable because of its tremendous medical benefit, ultimately for the patient's safety, finding a means to perform ionizing radiation imaging studies with the lowest possible radiation exposure is very desirable, while not limiting the imaging modalities' diagnostic capabilities. An even better scenario is that we can perform these biomedical imaging studies involving ionizing radiation with the lowest-possible radiation exposure, much lower than the dose levels of currently performed procedures, while we can enhance the diagnostic and prognostic value by unlocking visually hidden information using modern computational techniques. In this presentation, I will focus on our current understanding of how to lower radiation exposure from clinical PET studies, and shed some light on the ultimate limit, and how to apply and validate modern computational techniques to unlock the hidden image features that could present additional valuable information such as quantitative prognostic metrics.

Plenary Talk 2 **Time: 11:10-11:50 AM**

Biomimetic self-templating materials and application

Seung-Wuk Lee, Ph.D.
Professor at UC Berkeley
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In nature, helical macromolecules such as collagen, chitin and cellulose are critical to the morphogenesis and functionality of various hierarchically structured materials. During morphogenesis, these chiral macromolecules are secreted and undergo self-templating assembly, a biological manufacturing process whereby multiple kinetic factors influence the assembly of the incoming building blocks to produce non-equilibrium structures. A single macromolecule can form diverse functional structures when self-templated under different conditions. Collagen type I, for instance, forms transparent corneal tissues from orthogonally aligned nematic fibers, distinctively colored skin tissues from cholesteric phase fiber bundles, and mineralized tissues from hierarchically organized fibers. Nature's self-templated materials surpass the functional and structural complexity achievable by current top-down and bottom-up fabrication methods. However, self-templating has not been thoroughly explored for engineering synthetic materials.

In my presentation, I will demonstrate a facile biomimetic process to create functional nanomaterials utilizing chiral colloidal particles (M13 phage). A single-step process produces long-range-ordered, supramolecular films showing multiple levels of hierarchical organization and helical twist. Using the self-templating materials assembly processes, we have created various biomimetic supramolecular structures. The resulting materials show distinctive optical and photonic properties, functioning as chiral reflector/filters and structural color matrices. Through the directed evolution of the M13 phages, I will also show how resulting materials can be utilized as functional nanomaterials for biomanufacturing, biosensor, bioenergy, and biomedical applications

Plenary Talk 3 **Time: 11:50-12:30 PM**

A novel natural killer cell subset with potent anti-viral and anti-tumor activity

Sung Jin Kim, Ph.D.
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We have recently discovered a previously unknown subset of human natural killer (NK) cells that displays potent functional activity against tumor and virus-infected target cells in concert with target-specific antibodies. This novel NK subset is characterized by a deficiency in the expression of the signaling adaptor FcRgamma, and has therefore been termed "FcRgamma-deficient NK or g-NK cells." Intriguingly, g-NK cells are present in approximately 1/3rd of the healthy individuals tested, and their presence is associated with infection by human cytomegalovirus (HCMV), a common herpesvirus that causes asymptomatic infection in billions of people worldwide. Our study indicates that g-NK cells represent a new class of memory-type cells, which utilizes Ag-specific antibodies and the germline-encoded Fc receptor (CD16) for target recognition. Given that g-NK cells have been found in only a subgroup of the population, the presence or absence, as well as quantity, of g-NK cells may contribute to differences in disease susceptibility and progression among people, as well as immune response to antibody-based therapy. In this seminar, I will talk about adaptive immune features, non-human primate model, and therapeutic potential of g-NK cells in cancer treatment.

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RESEARCH TALKS #1

Mitochondrial ATP transporter depletion protects mice against liver steatosis and

Time: 1:40-2:00 PM

Joonseok Cho, Ph.D.
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insulin resistance

Non-alcoholic fatty liver disease (NAFLD) is a common metabolic disorder in obese individuals. Adenine nucleotide translocase (ANT) exchanges ADP/ATP through the mitochondrial inner membrane, and Ant2 is the predominant isoform expressed in the liver. Here we demonstrate that targeted disruption of Ant2 in mouse liver enhances uncoupled respiration without damaging mitochondrial integrity and liver functions. Interestingly, liver specific Ant2 knockout mice are leaner and resistant to hepatic steatosis, obesity and insulin resistance under a lipogenic diet. Protection against fatty liver is partially recapitulated by the systemic administration of low-dose carboxyatractyloside, a specific inhibitor of ANT. Targeted manipulation of hepatic mitochondrial metabolism, particularly through inhibition of ANT, may represent an alternative approach in NAFLD and obesity treatment.

Molecular scale engineering of membranes for efficient drug capture

Time: 2:00-2:20 PM

Hee Jeung Oh, Ph.D.
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Designing new membranes with a set of previously unachievable transport properties will have an enormous impact on many applications, including health-related devices, energy-efficient separations, and energy storage. The advancement of these technologies is highly dependent on polymer membranes which selectively transport only desired penetrants while maintaining chemical stability.

Molecular transport in polymer membranes is greatly influenced by chemical and morphological structures of polymers. Here designing highly structured polymer membranes for a new emerging biomedical application, "drug capture", to minimize the side effects of cancer drugs during chemotherapy, is discussed. The transport mechanism in polymer membranes is studied from the fundamental perspectives of polymer-penetrant interactions and templating diffusion pathways for selective transport of small molecules.

Coronary vessel sources during development sets tissue size and suppresses human disease phenotypes

Time: 2:20-2:40 PM

Siyeon Rhee, Ph.D.
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The process by which organs and tissues achieve appropriate size during development is a currently unresolved phenomenon. For example, the determinants that direct the mammalian heart wall to expand during development to support cardiovascular function are not entirely known. Defects in this process often result in the congenital heart disease, patients of which suffer from reduced fitness and survival. Here, we deleted the one of chromatin remodelers from different tissues in the developing heart and found that endothelial-specific knockouts resemble human heart disease. Furthermore, mutant hearts displayed defective angiogenesis from progenitors. *In vitro* heart cultures revealed that endothelial cells promote myocardial proliferation independent of oxygen delivery, which is defective in mutants. Mechanistically, chromatin remodeler gene supports angiogenesis by controlling proliferation during development. These data indicate that the extent of tissue vascularization is critical in determining the mammalian heart wall size and suppresses human disease phenotypes. These studies may inform strategies for tissue repair and regeneration.

Automated localization and classification of pulmonary nodules suspicious for lung cancer using generative models followed by 3D deep convolutional neural network

Time: 2:40-3:00 PM

Jae Ho Sohn, MD, MS
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Lung cancer is the leading cause of cancer mortality in the USA. Identification of suspicious pulmonary nodules is an important objective of lung cancer screening but remains time-consuming and repetitive for radiologists. Numerous computer aided detection systems have been proposed to this date, but excessive false positives remain an important barrier to widespread adoption. Recent advancement in deep learning has dramatically improved localization and classification task accuracy. Using generative models followed by 3D convolutional neural network (CNN), we develop and validate an improved nodule localization and classification system. We use 1600 CT studies from the National Lung Cancer Screening Trial. After automatically segmenting the lung fields, a subset of annotated nodules were resized, morphed, and transplanted into a segmented lung. Standard augmentation strategy was utilized to generate >1 million artificial nodules. Localization task was trained on a 3D fully convolutional CNN with all-convolutional neural network, resembling the U-net architecture. Pre-trained weights were transferred to a 18-layered 3D convolutional neural network inspired by the Network-in-Network architecture. Total training and cross-validation on NVIDIA K80 took 870 GPU-hours. The final model detected 57 out of 68 (83.8%) true cancer cases while correctly ignored all nodules in 66 out of 141 (46.9%) non-cancer patients. Exclusively in classification task, the model achieves AUC of 0.892. In conclusion, an automatic lung nodule localizer and classifier was developed using generative approach followed by CNN.

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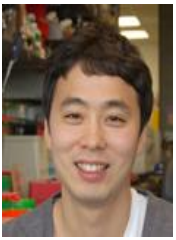
RESEARCH TALKS #2

Competing memories of mitogen and p53 signaling control cell-cycle entry

Time: 3:40-4:00 PM



Hee Won Yang, Ph.D.
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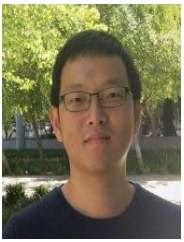
Newly born daughter cells decide to either enter the next cell cycle or exit to a quiescent state. Here, we show that cells make this fundamental decision based on competing memories of mitogen and stress signaling. Rather than erasing their signaling history at cell-cycle checkpoints before mitosis, mother cells transmit DNA damage-induced p53 and mitogen-induced cyclin D to newly born daughter cells. We show that the ability of daughter cells to activate Cdk4 is determined by an ultrasensitive stoichiometric relationship between cyclin D1 and the p53-induced Cdk inhibitor p21. Thus, daughter cells control the proliferation-quiescence decision by converting the memories of variable mitogen and stress signaling into a competition between cyclin D1 and p21 expression. We propose a cell-cycle control principle based on natural variation, memory, and competition that maximizes the health of growing cell populations.

Limited contribution of rare, noncoding variation to autism spectrum disorder from sequencing of 2,076 genomes in quartet families

Time: 4:00-4:20 PM



Joon Yong An, Ph.D.
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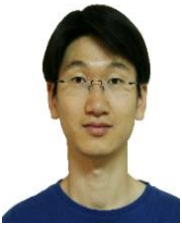
Genomic studies to date in autism spectrum disorder (ASD) have largely focused on newly arising mutations that disrupt protein coding sequence and strongly influence risk. We evaluate the contribution of noncoding regulatory variation across the size and frequency spectrum through whole genome sequencing of 519 ASD cases, their unaffected sibling controls, and parents. Cases carry a small excess of de novo (1.02-fold) noncoding variants, which is not significant after correcting for paternal age. Assessing 51,801 regulatory classes, no category is significantly associated with ASD after correction for multiple testing. The strongest signals are observed in coding regions, including structural variation not detected by previous technologies and missense variation. While rare noncoding variation likely contributes to risk in neurodevelopmental disorders, no category of variation has impact equivalent to loss-of-function mutations. Average effect sizes are likely to be smaller than that for coding variation, requiring substantially larger samples to quantify this risk.

Social control of hypothalamus-mediated male aggression

Time: 4:40- 5:00 PM



Taehong Yang, Ph.D.
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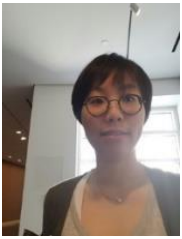
Social behaviors such as male territorial aggression are developmentally hardwired in the sense that they can be displayed without prior training. Nevertheless, activation of the underlying neural circuits requires both circulating sex hormones as well as conspecific sensory cues such as pheromones. How these external and internal cues modulate functional activity of the circuit is poorly understood. We have previously shown that progesterone receptor (PR) expressing neurons in the ventromedial hypothalamus (VMH) are essential for the display of male territorial aggression in adult mice. Here we examine the extent to which such male aggression
mediated by PR+ VMH neurons is regulated by internal physiological states and external social cues. We find that these neurons can drive aggressive displays in males independent of pheromonal input, circulating gonadal hormones, or opponents. By contrast, we find that social context exerts a dominant, over-riding influence to inhibit male territorial aggression even when PR+ VMHvl neurons are heterologously activated. In addition to these unpublished studies, I will also present findings that provide mechanisms whereby social context can inhibit male aggression. Together, my findings provide new insights into the influence of nature and nurture on the display of hardwired social interactions.

The role of Ninjurin1-p53 loop in tumorigenesis

Time: 4:40- 5:00 PM



Hee Jung Yang, Ph.D.
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The tumor suppressor p53 plays a pivotal role in maintaining genomic integrity and inactivation of the p53 pathway is known to be central for tumor development. We previously identified that nerve injury-induced protein 1 (Ninjurin1, Ninj1) is a target of tumor suppressor p53 and can in turn repress wild-type p53 expression *via* mRNA translation. Here, we showed that Ninj1 was capable of repressing mutant p53 expression also. Interestingly, though its regulation of wild-type and mutant p53, Ninj1 had opposing roles in modulating cell growth and migration. Briefly, cell growth and migration were inhibited by loss of Ninj1 in wild-type p53 containing cells, but were enhanced in mutant p53-containing cells. To further explore the role of Ninj1-p53 axis *in vivo*, we generated a cohort of Ninj1 compound mice by crossing Ninj1-deficiency mice with mutant p53R270H knock-in or p53-null mice. We found that when p53 was intact, mice deficient in Ninj1 developed severe systemic inflammation, but were not prone to spontaneous tumors, presumably due to the increased expression of wild-type p53. Importantly, in a mutant p53 background, Ninj1 deficiency shortened the life-span, increased tumor burden, and altered tumor spectra of p53R270H/- mice. Furthermore, in a p53-null background, Ninj1 deficiency significantly increased the penetrance of thymic T-cell lymphoma. Together, our data suggest a critical role of Ninj1 in modulating the inflammatory response and tumorigenesis, thus the Ninj1-p53 axis may be explored for inflammatory diseases and cancer treatment.

Comprehensive molecular profiling of single circulating tumor cells from lung cancer patients

Time: 5:00- 5:20 PM

Seung-Min Park, Ph.D.
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Circulating tumor cells (CTCs) are established cancer biomarkers for the "liquid biopsy" of tumors. Molecular analysis of single CTCs, which recapitulate primary and metastatic tumor biology, remains challenging because current platforms have limited throughput, are expensive, and are not easily translatable to the clinic. Here, we report a massively parallel, multigene-profiling nanoplatform to compartmentalize and analyze hundreds of single CTCs. After high-efficiency magnetic collection of CTC from blood, a single-cell nanowell array performs CTC mutation profiling using modular gene panels. Using this approach, we demonstrated multigene expression profiling of individual CTCs from non–small-cell lung cancer (NSCLC) patients with remarkable sensitivity. Thus, we report a high-throughput, multiplexed strategy for single-cell mutation profiling of individual lung cancer CTCs toward minimally invasive cancer therapy prediction and disease monitoring.

There exists an urgent need for minimally invasive molecular analysis tools for cancer assessment and management, particularly in advanced-stage lung cancer, when tissue procurement is challenging and gene mutation profiling is crucial to identify molecularly targeted agents for treatment. High-throughput compartmentalization and multigene profiling of individual circulating tumor cells (CTCs) from whole-blood samples using modular gene panels may facilitate highly sensitive, yet minimally invasive characterization of lung cancer for therapy prediction and monitoring. We envision this nanoplatform as a compelling research tool to investigate the dynamics of cancer disease processes, as well as a viable clinical platform for minimally invasive yet comprehensive cancer assessment.

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