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Non-Fungible Tokens for Organoids: Decentralized Biobanking to Empower Patients in Biospecimen Research

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Abstract

Introduction: Scientists use donated biospecimens to create organoids, which are miniature copies of patient tumors that are revolutionizing precision medicine and drug discovery. However, biobanking platforms remove donor identifiers to protect privacy, precluding patients from benefiting from their contributions or sharing information that may be relevant to research outcomes. Decentralized biobanking (de-bi) leverages blockchain technology to empower patient engagement in biospecimen research. We describe the creation of the first de-bi prototype for an organoid biobanking use case.

Methods: We designed and developed a proof-of-concept non-fungible tokens (NFTs) framework for an organoid research network of patients, physicians, and scientists within a synthetic dataset modeled on a real-world breast cancer organoid ecosystem. Our implementation deployed multiple smart contracts on Ethereum test networks, minting NFTs representing each stakeholder, biospecimen, and organoid. The system architecture was designed to be composable with established biobanking programs.

Results: Our de-bi prototype demonstrated how NFTs representing patients, physicians, scientists, and organoids may be united in a privacy-preserving platform that builds upon relationships and transactions of existing biobank research networks. The mobile application simulated key features, enabling patients to track their biospecimens, view organoid images and research updates from scientists, and allow physicians to participate in peer-to-peer communications with basic scientists and patients alike, all while ensuring compliance with de-identification requirements.

Discussion: We demonstrate proof-of-concept for a web3 platform engaging patients, physicians, and scientists in a dynamic research community, unlocking value for a model organoid ecosystem. This initial prototype is a critical first step for advancing paradigm-shifting de-bi technology that provides unprecedented transparency and suggests new standards for equity and inclusion in biobanking. Further research must address feasibility and acceptability considering the ethical, legal, economic, and technical complexities of organoid research and clinical translation.

Plain Language Summary

Scientists create miniature copies of patient tumors called organoids for precision medicine research, but privacy policies preclude communication of relevant findings with patients and their physicians. We propose blockchain infrastructure to connect patients, scientists, and physicians, eliminating barriers between bench and bedside while ensuring regulatory compliance. Our decentralized biobanking (de-bi) prototype utilizes non-fungible tokens (NFTs) to represent stakeholders, specimens, and organoids in a privacy-preserving platform. Patients are empowered to track specimens, access updates, and engage as collaborators, creating new standards for transparency, equity, and inclusion. Ongoing work addresses ethical, legal, and technical challenges to realizing the patient-centered biobanking revolution.

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Organoid technology creates living copies of donated patient tumors, revolutionizing precision medicine and drug development.[1,2] These next-generation biobank products enable high-throughput screening of investigational new drugs and FDA-approved therapies, advancing generalizable discovery while producing potentially life-saving insights for the respective donor. Stunning images of these human cancer models are captured in the process, showcasing their uniqueness and documenting treatment responses.

Validation and development of patient-derived organoids require long-term clinical data and linked specimens. Delivering translational impact necessitates protocols for connecting the bench and bedside. However, current biobanking platforms remove patient identifiers from donated specimens to protect privacy, yielding organoid ecosystems without mechanisms for patients and scientists to communicate information that may be critical for health or research outcomes.[3]

Decentralized biobanking (de-bi) applies blockchain technology and web3 values to embed transparency, accountability, and inclusion in biomedical research.[4] Our bioethics-driven technology framework leverages non-fungible tokens (NFTs) to keep patients connected to their biospecimens throughout the research lifecycle.[5] Minting NFTs to represent patient-derived organoids could open communications between scientists and patients via a privacy-preserving platform composable with existing biobank and research protocols. If successful, our approach will advance patients' rights to share in knowledge, health, and financial benefits of their research contributions.[6]

We discuss the development of an alpha prototype that applies NFTs to empower patients as stakeholders in organoid research. Our approach establishes public, immutable relationships between patients, their biospecimens, and organoid derivatives, as well as a related network of physicians, scientists, biobanks, and research protocols.[7] We hypothesized that organoid images could be leveraged as de-identified artworks and represented with NFTs on a public blockchain, demonstrating proof-of-concept for peer-to-peer transactions between scientists and patients that preserve privacy and add utility for building meaningful research communities.[8]

Methods

Organoid Ecosystem Mapping

We interviewed U.S. breast cancer patients, physicians, translational scientists, and biobankers throughout 2021 and visited all representative sites in our local biospecimen procurement supply chain to inform our understanding of the current organoid ecosystem. This enabled the development of a high-fidelity simulated model dataset representative of a real-world breast cancer surgical program linked to a biobanking platform and downstream organoid ecosystem.

We mapped stakeholder relationships and activities across the biospecimen research lifecycle to define key ecosystem components for the organoid biobanking use case, with a focus on the flagship breast cancer organoid program at the Institute for Precision Medicine (Figure 1). Qualitative interview data and subsequent user-experience design research related to patient engagement in our NFT Biobank Platform will be reported elsewhere.

The current organoid biobanking process depicted here incorporates three distinct domains: the clinical setting, the biobanking platform, and the organoid ecosystem.

1. Clinical setting: Patient provides broad consent[9] for research biobanking during consent for cancer surgery. They undergo surgery, whereupon tissue is sent to the pathology lab, histology analysis is performed, and clinical results are returned to the patient and their clinicians via EMR.

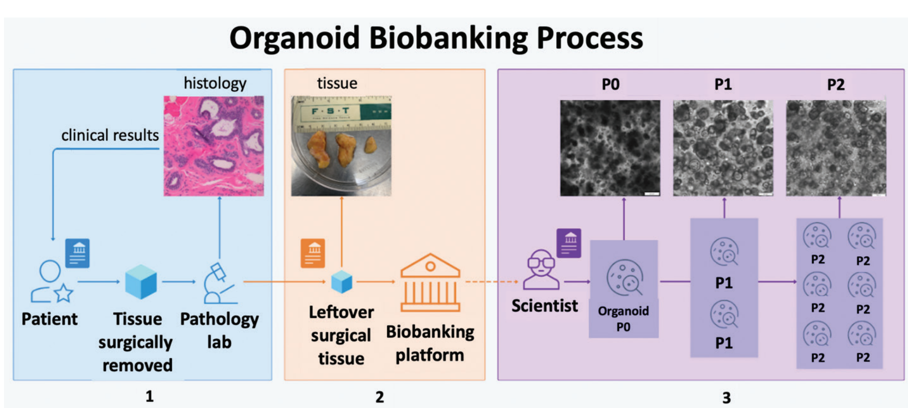

Fig. 1. Organoid biobanking process flow diagram demonstrating (1) patient-facing clinical setting, (2) biobanking platform functions, and (3) specimen procurement and handling for the organoid ecosystem, with representative images from each domain. Images courtesy Institute for Precision Medicine.

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2. On the day of surgery, the surgical team communicates with research staff to coordinate real-time retrieval of leftover tissues from the pathology lab. These tissues are transferred from the clinical setting to the biobank under an institutional review board (IRB)-approved biobanking protocol. Specimens are processed and de-identified in the biobank and then either distributed immediately to a designated organoid lab or frozen for future research.
3. Organoid ecosystem: Scientists obtain an IRB-approved protocol for organoid research, granting access to the biobanking platform. They communicate with surgeons to earmark upcoming cases of interest. Scientists are notified when tissues are sent from the operating room to the pathology lab. Within the hour, they collect the leftover tissues from the biobank while the cells are still alive. The tissues are processed in the research lab, enabling the patient's cells to be grown in 3D culture medium and expanded via a multigenerational organoid development process. Each organoid generation is imaged, and individual units may be shared for use in experiments, used to grow more copies, or may be frozen for future research.

Foundational research on the breast cancer biobanking process informed technical requirements for a web3 prototype that would enable ongoing patient engagement in organoid research and development activities. We sought to utilize the images created in the organoid process to represent complex activities to patients in a transparent and accessible manner. Our team was authorized to use organoid research images and associated de-identified metadata to animate our proof-of-concept prototype, lending photorealistic elements to our experimental data and app demonstrations. Further details and survey data related to our proposal to use organoid images as "tokens of appreciation" for respective biospecimen donors will be described elsewhere.

Platform Design

The core conceptual design of a "de-bi" platform was created to guide the priorities, goals, and features for prototype development. The system concept required a privacy-preserving NFT biobanking framework that connects patients, scientists, and physicians for research engagement and dynamic data sharing (Figure 2). The "de-bi" system design demonstrates three core stakeholders: patient, scientist, and physician, each connected through a common biobanking platform. Data flow bidirectionally between stakeholders on a peer-to-peer basis, as each can make data requests and initiate data sharing with the other. Importantly, transparency, accountability, equality, and inclusion in the de-bi ecosystem are embedded by design.

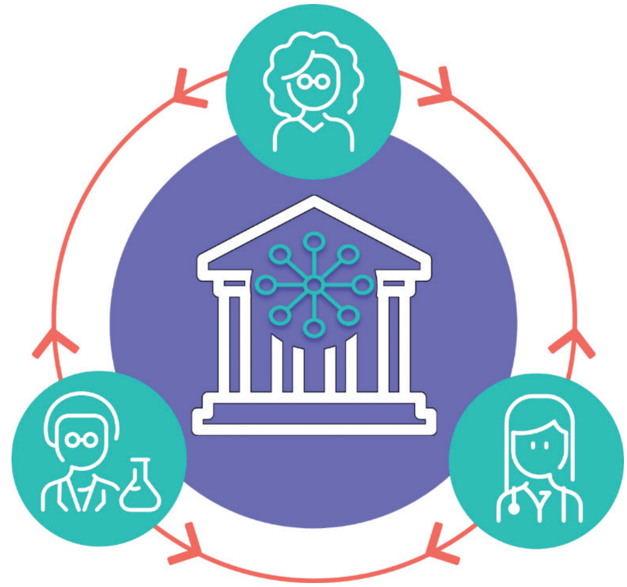

Fig. 2. Decentralized biobanking ecosystem concept diagram.

Our approach advanced beyond current methods for implementing access management and dynamic consent for biological data[10,11] by utilizing initial consent procedures as a basis for enabling a platform for rich longitudinal community engagement among stakeholders that would otherwise remain siloed after initial permissioned transactions. The application of NFTs to represent the unique participants and assets exchanged on the biobanking platform was critical for enabling a suite of participatory, value-adding features and creating a basis for a gamified research ecosystem that aligns incentives and rewards pro-social behaviors.

To advance a functional prototype, a simulated dataset was developed to reflect specifications and activities pertaining to breast cancer biobanking, with the generation of organoids and related derivatives (e.g., genomics data). Our synthetic dataset is modeled from a subset of the Breast Disease Research Repository at the University of Pittsburgh and Lee-Oesterreich Lab Data to be representative of a real-world breast cancer organoid biobanking ecosystem. The model sought to represent a diversity of breast cancer subtypes, disease stages, biological patient characteristics, and cellular and molecular phenotypes driving contemporary research paradigms. We represented all stakeholder classes with one or more individuals or research entities in each role. A schematic of the data forms for each stakeholder and their relationships created for our NFT organoid ecosystem prototype is depicted in Figure 3.

We followed best practices regarding the creation of decentralized applications that leverage blockchain as part of their solutions while relying on a hybrid approach that

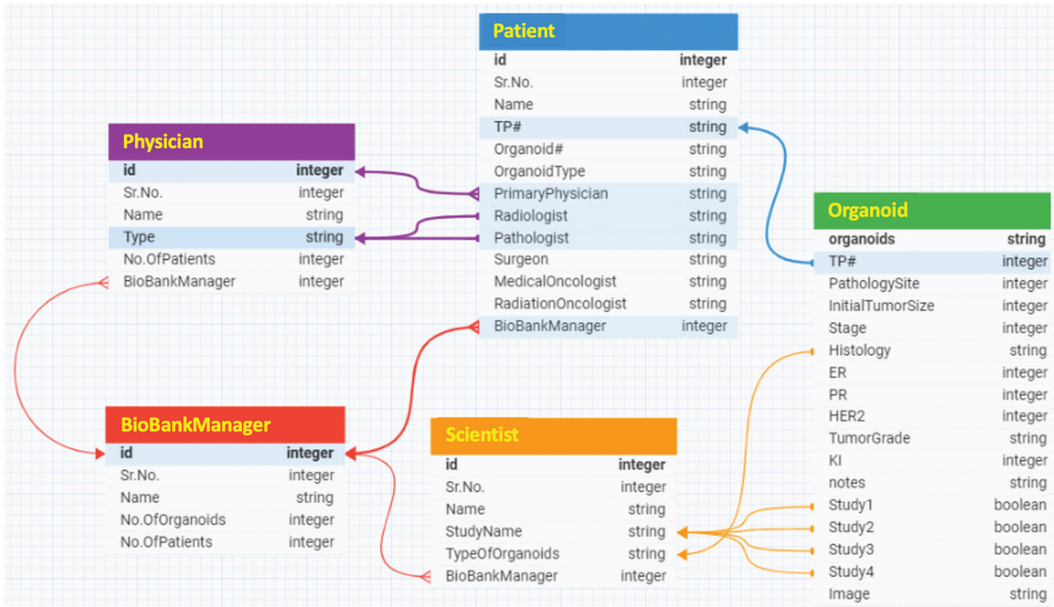

Fig. 3. Simulated de-bi organoid ecosystem dataset schematic.

benefits from the flexibility and iterative capabilities of centralized software platforms.[12] Tokens representing the stakeholders, biospecimens, and organoids will be stored on-chain. Sensitive, donor-specific details will remain on centralized databases on institutional servers, applying a multi-layered approach from a proposed Reference Architecture for Blockchain (REF-ArcBC) for establishing a standardized, efficient, and secure foundation for developing and implementing blockchain solutions.[12] While the NFT framework will provide a decentralized backbone for the application, in-app user activity data will also remain centralized on de-bi servers, reducing gas fees and transaction costs by minimizing the use of on-chain data storage, promoting adoption by limiting data privacy concerns and optimizing efficiency by focusing tokenization on high impact, low-frequency transactions.

Blockchain Network Selection

Deciding which blockchain to build on was a crucial step to set the foundation for our solution as each blockchain offers different primary features along with a built-in community and culture. Nearly all blockchain applications and proof-of-concepts in the medical and biobanking space make use of private or permissioned blockchains, such as Hyperledger Fabric.[13,14] Departing from this trend, we chose to build our proof-of-concept for “de-bi” on the public, decentralized Ethereum Blockchain Network. de-bi is designed as an open-source public good that facilitates the exchange of de-identified biological assets to enable new forms of research collaboration without displaying accompanying identifiable data. The system maintains compliance with established biobanking methods while empowering the inclusion of patients who lack access to internal databases and creating an ecosystem that is open to all public and private sector contributors, advancing shared goals for human health and wellbeing.[15]

Ethereum is a worldwide system, an open-source platform to write computer code that stores and automates digital databases using smart contracts without relying upon a central intermediary, solving trust with cryptographic techniques.[16] As the first to introduce the concept of smart contracts and NFTs, Ethereum was the most popular chain to build on and the most commonly used chain for both decentralized finance and NFTs at the time of our proof-of-concept development in 2021–2022. It featured the most mature development ecosystem, offering a wide range of available tools, standards, and resources for developing dApps (decentralized applications). Additionally, we were drawn to Ethereum because the values of the creators aligned with our focus on ethical, inclusive, and transparent collaboration.

There are downsides to building our prototype on Ethereum that we needed to consider. At the time of implementation, Ethereum used a Proof of Work consensus mechanism that incentivizes validation by rewarding miners for adding computational power to secure the network. This incentive is delivered in the form of gas fees[17] required to execute any transaction, which can be increased to entice miners to validate a user’s transaction sooner. Gas prices are dependent on network congestion and demand, making them highly susceptible to market volatility.[17] This variable cost was taken into account in our design of the NFT framework, as noted above, and

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will require continuous monitoring and assessment as we advance our solution to ensure that the cost of using this technology is not prohibitive for our end users.

System Architecture

The de-bi application consists of three main components: a decentralized peer-to-peer blockchain infrastructure, a client mobile application, and a service application, as shown in Figure 4. The architecture of the proposed system and its working principle are illustrated through a detailed description of these core components and the channels of communication connecting them. Figure 4 illustrates the following components:

1. Client: Mobile Flutter application with frontend user interfaces for patient and scientist, as well as physician and biobanker (the latter two are not shown in Figure 4).
2. Service Application: A NodeJS API (Application Programming Interface) processes blockchain-related service requests by sending a transaction to an Infura-hosted node, which broadcasts transactions to the remaining nodes in the system. Additionally, a cloud-hosted Firebase Database and API for storing all off-chain data, such as user records and in-app activity logs.
3. Blockchain Infrastructure: Rinkeby and Ropsten Ethereum test networks act as our decentralized, peer-to-peer infrastructure, providing the environment for our suite of ERC-721 smart contracts, which mint the unique non-fungible tokens (NFTs) representing stakeholders, biospecimens, and organoids.

NFT Framework

By creating a digital ecosystem of NFTs representing stakeholders, biospecimens, and derivatives within real-world research networks, we establish connections and communication channels that were not possible in the current landscape. This NFT framework acts as a foundation for an open-source decentralized biobanking system, enabling new applications for donor engagement, enhancement of pre-clinical research, and direct return of clinically relevant information.[18] If successful, the framework will ultimately support a sustainable and ethically governed decentralized marketplace solution that maximizes the distribution of unused biospecimens to advance precision medicine.

We developed multiple smart contracts with Solidity, a statically typed curly-braces programming language designed specifically for developing smart contracts for the Ethereum network. They were initially deployed to a local blockchain called Ganache before transitioning them to the Rinkeby test network for Ethereum. To deploy to an Ethereum network, our Node.JS application sends a signed transaction via an Externally Owned Account (EOA) within a wallet[12]—a digital tool that allows users to store and manage their cryptocurrencies while providing private and public key pairs for transactions to an Infura hosted node, which broadcasts our transaction to the entire network.

Our smart contracts were written following the ERC-721 standard for NFTs, enabling the minting of NFTs as unique, cryptographic representations of patients, scientists, physicians, and biobankers as collaborative stakeholders within our proposed ecosystem. To receive these tokens, users will require an EOA controlled with private keys. This is typically done via the wallet interface of third-party providers like Metamask.

NFTs were also created to represent biospecimens and established organoids, but their properties were customized to include the unique identifier of the token

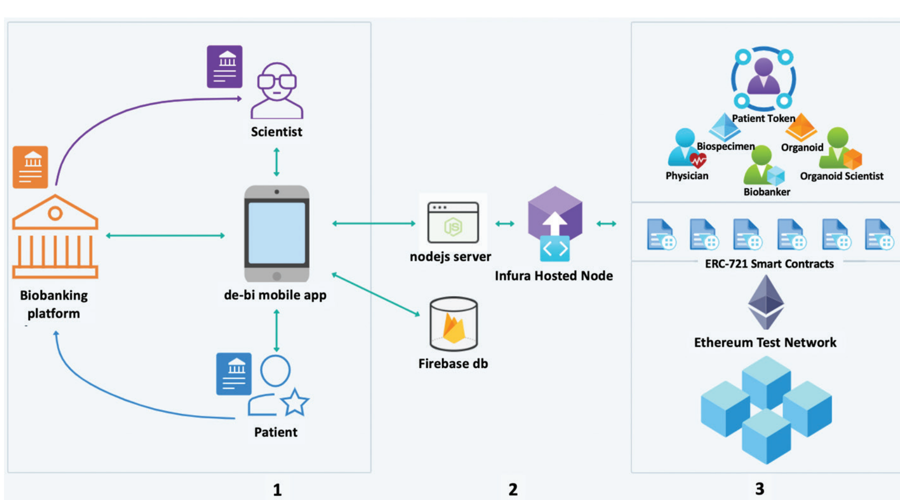

Fig. 4. System architecture diagram for decentralized biobanking enabled organoid research.

representing their donor. By mapping this relationship on-chain, patients can remain permanently connected to their donations. This immutable, transparent connection creates opportunities for open communication channels with other stakeholders who interact with their donated samples. As these tokenized assets are only displayed as digital hash, these channels can facilitate a collaborative exchange of information without exposing any personal patient details. We showcase the potential by displaying real organoid images to the patient and all other stakeholders in our simulated biospecimen research ecosystem. Real organoid images were assigned to represent specific model organoids from individual patients in our synthetic dataset and were stored on Firebase.

Frontend Design and Development

Preliminary wireframe designs were developed in collaboration with real potential users and through content analysis of representative biobank data and organoid research artifacts. We drew inspiration from feature elements frequently implemented in popular mobile applications for banking, social media, and gaming to inform the development of a skeuomorphic user experience with familiar components applied to a novel context. We designed and developed a Flutter mobile application connected to a Firebase Database to conceptualize the activities and workflows of each represented stakeholder in our proposed framework. Standard libraries were used to design elements. We performed live demonstrations of the functional de-bi prototype with patients, scientists, physicians, and biobanker user groups between 2021 and 2022.

Results

Model Organoid Biobanking Ecosystem

The simulated dataset was developed in collaboration with the Institute for Precision Medicine Pitt Biospecimen Core and modeled to reflect detailed specifications and activities of the Breast Disease Research Repository, a large breast cancer biobanking platform. Key variables for effectively discovering organoids and related specimens were incorporated to optimize performance in clinical and pre-clinical research use cases. Representative user personas were developed in collaboration with the Lee-Oesterreich Lab and the Institute for Precision Medicine breast cancer organoid biobank. Our simulated stakeholders included seven patients, one biobanker, four scientists, and 17 collaborating physicians representing various breast cancer subspecialties (Table 1). The patients in our dataset contributed 12 unique organoids representing various breast cancer features, which were in use for four different study protocols (Table 2).

Table 1. Overview of stakeholder dataset: Descriptive demographics for patients, scientists, physicians, and biobankers modeled in our decentralized biobanking prototype

Simulated stakeholder overview

User (#)	Metric	Descriptive Demographics
Patients (7)	Clinical stage (tissue diagnosis)	Primary (3)
		Metastatic (3)
		Benign (1)
	Organoids per patient (n)	1 organoid—3 patients
		2 organoids—3 patients
		3 organoids—1 patient
	Studies per patient (n)	1 study—3 patients
		2 studies - 4 patients
Scientists (4)	Research study focus	Study 1—Primary tumors
		Study 2—Metastatic lesions
		Study 3—Primary and Mets
		Study 4—Normal breast tissue
	Average patients per study (n)	3.75 (range 2–5) patients/study
	Organoids in each study (n)	Study 1–5
		Study 2–4
		Study 3–7
		Study 4–2
Physicians (17)	Physicians per type (n)	Primary (5)
		Radiologist (2)
		Pathologist (2)
		Surgeon (4)
		Medical oncologist (3)
		Radiation oncologist (1)
	Average patients by type (n)	Primary 1.4
		Radiologist 3.5
		Pathologist 3.5
		Surgeon 1.75
		Medical oncologist 2.33
		Radiation oncologist 7
Biobankers (1)	Patient cases processed	Patients (7)
	Relationships managed	Scientists (4)
		Surgeons (4)
		Pathologists (2)
		Medical Oncologists (2)
	Organoid copies distributed (n)	18

Functional Prototype Applications

The functional mobile application demonstrated several key features for model patients, biobankers, scientists, and physicians within the simulated biobank ecosystem. Account creation and sign-in, as well as visibility to the collective organoid gallery for a given research study, was enabled for all users. Key features developed for each stakeholder group are included below.

Table 2. Overview of Organoid Dataset: Descriptive demographics for patient-derived organoids modeled in our decentralized biobanking prototype

Dataset (n)	Metric	Descriptive demographics
Organoids (12) represented	Pathology site	Primary breast tumor (5)
		Metastatic—Liver (1)
		Metastatic—Lung (1)
		Metastatic—Lymph Nodes (1)
		Metastatic—Brain (1)
		Benign breast tissue (3)
	Histology	Invasive Ductal Carcinoma—7
		Invasive Lobular Carcinoma—2
		Benign—3
	Estrogen receptor status	Negative—4
		Weak—1
		Mod—2
		Strong—2
		N/A—3
	Progesterone receptor status	Negative—4
		Weak—2
		Mod—2
		Strong—1
		N/A—3
	HER2 status	Negative—7
		Weak—0
		Mod—1
		Strong—1
		N/A—3
	Tumor grade	Low (G1)—3
		Moderate (G2)—2
		High (G3)—4
		N/A—3

N/A: not available.

Patients

1. Review and agree to terms of use, that is, provide informed consent for sharing organoids.
2. Store and update comprehensive cancer, medical, reproductive, surgical, and family history.
3. View NFT biowallet with images and information about their biospecimens and organoids.
4. View research studies that are using their donated biospecimens.
5. View research studies they may join to donate specimens based on research interests.
6. View organoid images and chat with other study participants in a "co-Lab" community forum.
7. Exchange 1-to-1 messages with scientists, biobankers, and physicians.
8. Share clinical history details with physicians and scientists in the biobank network.

Figure 5 demonstrates key features for patients on the decentralized biobanking application, including (1) home screen with informed consent, (2) biowallet with asset tracking, and (3) study-specific "co-lab" community.

1. Home page with informed consent pop-up: This view presents the overall framework of the patient UX, including a key step for both joining the platform or sharing organoids for any new research study, in which the donor reviews and accepts Terms and Conditions relevant to the proposed activities, mirroring traditional informed consent.
2. Biowallet: Demonstration of NFT biodata framework, encompassing various biological data assets collected, stored, and distributed by the biobank, including organoids, blood and tissue.
3. Organoid Co-lab: De-identified gallery of organoid images representing profile pictures of corresponding patient participants in a given study, with a forum for de-identified peer engagement.

Biobankers

1. Add records of new samples and organoids, which include a unique identifier for the donor, details about the specimen, and associated related images.
2. View and respond to scientists' requests for specimens or organoids.
3. Assess newly approved research protocols for potential matches with available organoid and biospecimen inventory.
4. Exchange 1-to-1 messages with scientists, physicians, and patients.
5. Biobankers were key players in the NFT biobank ecosystem, as their buy-in is critical for opening patient access to biospecimen collections and activities currently managed in siloed institutional databases. Record creation by the biobanker triggers a signed transaction to mint sample or organoid tokens, storing the unique identifier that establishes an immutable relationship with the donor. We demonstrate how our approach may create opportunities for biobankers to find users for their available inventory, facilitating more coordinated activities and laying a foundation for a marketplace network model. While these processes were manual for our prototype's small, simulated dataset, API or Oracle integrations would enable the automation of decentralized biobanking applications for biobankers in future iterations.

Scientists

1. Add new studies with descriptive information and educational resources to recruit patients from within the biobank donor community.

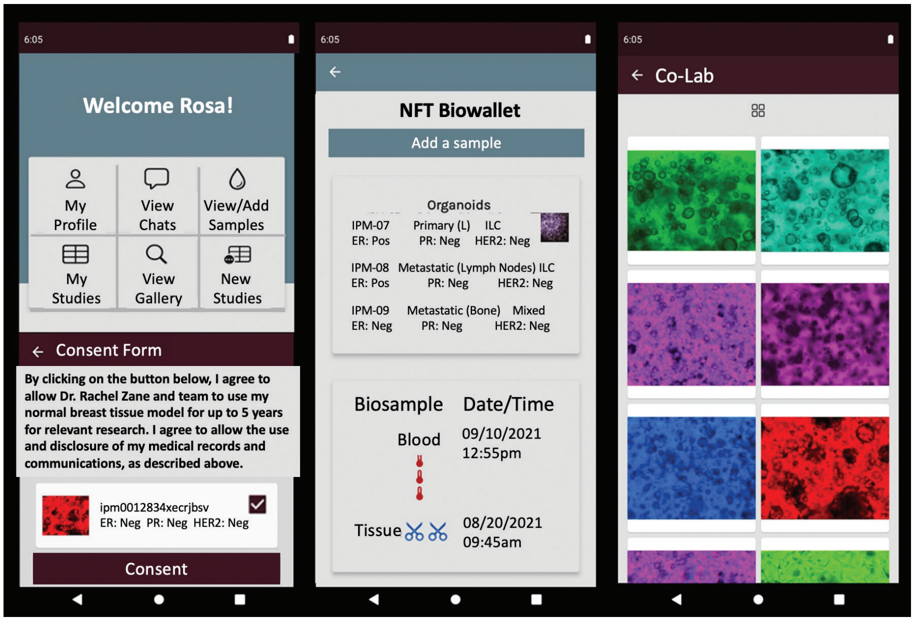

Fig. 5. User interface/user experience walkthrough for patient users. NFT: non-fungible token.

2. View studies, add study details, and share progress or related content from their research studies with study participants.
3. View available organoids and linked biospecimens within the biobank inventory.
4. Exchange 1-to-1 messages with patients, biobankers, and physicians.

Figure 6 demonstrates key features for scientists, including (1) creating a study token, (2) displaying study information, and (3) 1:1 chat function demonstrating communication between scientist and physician.

1. Add study token: Allows scientists to include patient-friendly content and leverage existing research communications to engage prospective and consented participants.
2. Research study token: Demonstration of high-level study synopsis, embedded video content, built-in FAQ, link to study participant forum, and ability to prompt 2-way messaging with patients or physicians.
3. Two-way messaging: Permissioned chat feature that allows both audio and written communications, with user identity displayed in accordance with specified permissions (i.e., scientists can chat with named physician collaborators, but communications with patients are always de-identified).

Physicians

1. Exchange 1-to-1 messages with patients, biobankers, and scientists
2. View profiles and access clinical details entered by their patients within the de-bi system.
3. View a sortable patient list that may be filtered or searched based on clinical criteria, biospecimen availability, and participation in particular research studies.

Though the physician features represented a relatively small component of the functional application, including physicians as stakeholders will be essential for protecting patients' interests in the NFT biobank ecosystem. Physician permissions within this system were role-based and directly corresponded to mutually validated clinical relationships between patient and physician users. Ultimately, granting physicians access to research on organoids created from their patients' donations will be critical for enabling translational research findings to be imputed into patient care in real-time.

Technical Challenges

The team encountered issues when deploying smart contracts to the Rinkeby testnet. Local deployment on Ganache was averaging 0.0006 eth, but the cost to deploy on Rinkeby was 5.8eth at the time. This prompted the shift to the Ropsten network, where deployment cost was closer to Ganache. We investigated the cause of this spike in gas cost[17] and the discrepancy between networks, and while the exact mechanism was unclear, it was believed to be due to a vulnerability in the design of the smart contract. This experience highlighted the challenges of relatively inflexible smart contract architectures and warranted caution for future prototype deployments, especially as we move to Ethereum Mainnet.

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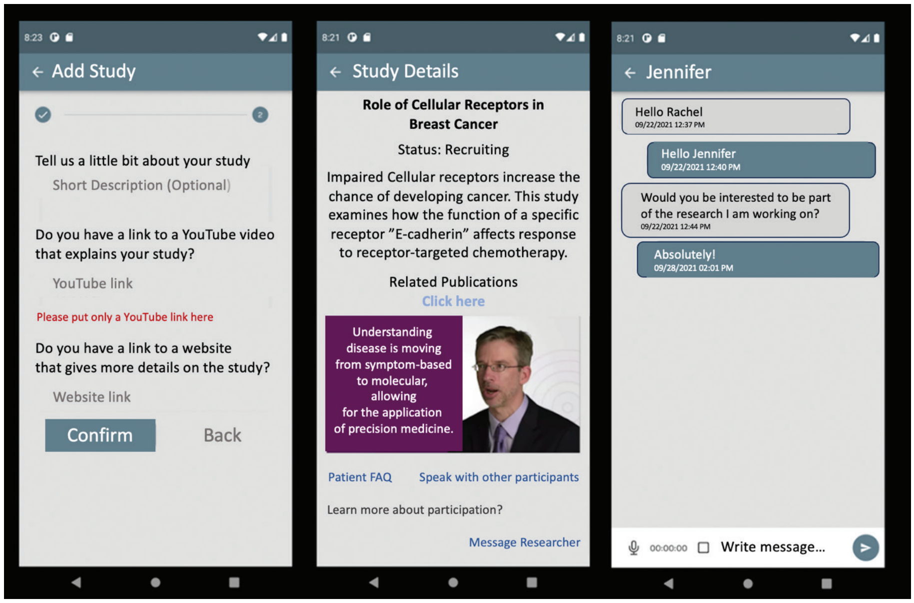

Fig. 6. User interface/user experience walkthrough for scientist users.

Discussion

Our initial prototype of a "de-bi" platform successfully demonstrates proof-of-concept for a paradigm-shifting use of blockchain technology to promote authentic transparency, community engagement, and dynamic collaboration in biospecimen research. The mobile application features and user interfaces reflect the needs of key stakeholders, informed by a highly representative model dataset encompassing key activities of a breast cancer organoid biobanking program. Through the representation of stakeholders with NFTs and the creation of a public, immutable relationship between patients, donated biospecimens, and derived organoids, the prototype suggests the potential for a decentralized framework to empower patients, unlock value, and enrich research. As NFTs are unique, cryptographic assets displayed as a digital hash, relationships mapped to the donated specimen can establish a transparent, privacy-preserving collaboration network that never reveals patients' identities. Our model is composable with existing biobank and research protocols that leverage de-identified specimens, demonstrating the possibility of integrating our proposed intervention for established biospecimen collection, procurement, and research processes.

Additionally, we simulate a mechanism to provide personalized feedback from the bench to the bedside in the form of real images captured during research and development of patient-derived organoids. The application also demonstrates the potential of a decentralized biobanking framework to support patient education, diversity, and engagement in research collaborations via a system that embeds assurances of trust, equity, and inclusion.[19]

Critically, our proof-of-concept for communication between scientists, patients, and their physicians creates opportunities for direct translation of clinically actionable research findings and for long-term enrichment of sample data with clinical context that participating patients or physicians may share.

Blockchain in Healthcare

Many other blockchain application prototypes in the medical and biobanking space make use of private or permissioned blockchains,[13] such as Hyperledger Fabric.[14] In private blockchains, only a limited number of participants, typically nominated by administrators, can participate in the network. This centralization of power over consensus mechanisms, participants, and processes removes the need for gas, as malicious entities are easily detectable and reprimanded. Central authorities can also enforce access restrictions to transactions at their discretion, making it easier to protect sensitive information within the network. It seems that permissioned blockchains such as Hyperledger can enable the development of efficient, cost-effective, and compliant software solutions within heavily regulated industries such as healthcare, and we can understand why many projects have gravitated toward this type of network.

However, a permissioned blockchain that does not strictly enforce immutability, traceability, and transparency across institutional boundaries may be insufficient for enabling a disruptive solution aimed at changing the paradigms of accountability for biobanking activities within a network of stakeholders who have been insulated from patient engagement via the de-identification process.

A system where every institution, service line, and research lab controls their own decentralized chain to store their respective biobanking samples fundamentally contradicts the belief that biospecimens are public goods and does not address the fundamental misalignment of incentives[20] that underlie siloing of biospecimen resources and related disjointedness of the biobanking ecosystem. For example, patients may move or travel to various localities for cancer treatment, indicating the importance of a cross-institutional approach, both for delivering comprehensive transparency of biobanking activities to patients and for maximizing scientists' access to a dynamic and growing set of health information relevant to their research.

Patient Engagement in Research

Alternative approaches to develop technologies for improving patient engagement in research are focused on clinical research,[21] where patients are active participants. By contrast, most organoid research activity uses de-identified samples, and translational scientists are not accustomed to communicating with patients, who may not be aware of the nature of their contributions to biobanking after one-time broad consent. We leverage colorized versions of real organoid images captured in the development of human cancer models as personalized "tokens of appreciation" for research participants: an initial bench-to-bedside data transaction that harnesses the visual, accessible, and appealing nature of images without creating undue clinical or financial liability. Key questions remain regarding the optimal design of the communication, image, and data sharing, and research engagement features for patient participants in the de-bi framework.

We believe that bringing transparency to translational research[19] will increase recruitment and rebuild trust. The community-engaged approach will be especially critical for promoting biospecimen donation among communities for whom distrust of established healthcare systems is a serious barrier to participation. The inborn uniqueness, immutable provenance, and decentralized ownership that is inherent to human tissues can be represented in an NFT-based system that respects patient rights, maximizes research benefits, and enables precision medicine. Forthcoming publications about patient acceptability of decentralized biobanking will highlight key value propositions with rich qualitative and quantitative data. Our upcoming pilot exercises will seek to define key metrics that will be essential to quantifying the effectiveness of our approach and justify further investment to enable scaling to broader populations and use cases.

Study Limitations

Our proof-of-concept prototype demonstrates the potential for a web3 platform that engages patients, physicians, and scientists in a privacy-preserving organoid community.

However, experimentation on additional key components and processes is still required to confidently assess the feasibility and acceptability of our technical approach. A reliable onboarding process that effectively verifies donor identity[22] to establish their relationship with the correct samples and that is accessible to diverse populations with varied technology, and health literacy is an integral part of our proposed framework that must be explored and confirmed in future prototypes. To propose an acceptable on-ramp for patients, we must adapt our systems to the regulations, preferences, and risk tolerances of the IRBs.

Additional suggestions for best practice in the live development of a production-ready solution include strategic design to address variable gas costs that are susceptible to volatility with market congestion, proving cost-prohibitive at a specific point in time on the Rinkeby test net. A live implementation will require a more thorough preliminary assessment of market conditions and existing gas costs across test networks and Mainnet to project accurately. There are additional requirements for security analysis[23] to identify and resolve any smart contract vulnerabilities and potential points of failure for maintaining the de-identification of human subjects and related organoids due to the sensitive nature of biomedical data. These strategies include a focus on data minimization, application of zero-knowledge proofs, and thorough security audits and penetration testing to identify and mitigate vulnerabilities.[12] Importantly, patients remain de-identified within our proposed NFT-biobanking system, demonstrating provisional compatibility of this approach with established HIPAA and GDPR[24] regulations.

In our initial prototype, organoids and the specimens from which they are derived are represented as discrete assets rather than derivative products with multiple complex functions and regenerative features. Further research will advance the sophistication of the smart contracts and tokens used to represent the creation, growth, and distribution of organoids as a critical step for building the foundation for pragmatic utility for the scientific community. Additionally, the access control mechanism for the mobile application prototype simulated roles/permissions to demonstrate on-chain ownership[16] of stakeholder, specimen, and organoid tokens. Real-world implementation will require these onboarding mechanisms. In our second proof-of-concept prototype, we developed a web application that implements stakeholder onboarding and expands the functionality of organoid tokens to more accurately reflect real-world activities, such as creation from a donated biospecimen. A subsequent technical report will advance the concepts and technical challenges relevant to a fully functional decentralized biobanking platform for organoid research.

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This prototype is limited as our simulation study did not engage real patients as direct users of the demo application. This step to deploy and test our framework with each stakeholder group will be essential to gather feedback, evaluate our assumptions, and inform future design and development. The simulation relied on manual user inputs (e.g., patient entry of extensive health information during the onboarding process), which represents an additional fraction and potential source of data corruption or correction, with no ready mechanism to discern the difference. A functional prototype fit for pilot deployment will require further development of mechanisms to integrate with and ensure interoperability across diverse institutional platforms.[12] Continued use of their existing systems is critical for easing adoption and maintaining compliance with current regulations.[25]

Additionally, this initial prototype was developed prior to significant advances in Layer 2 solutions to minimize the costs of token minting and related transactions. The feasibility and scalability of our NFT framework will rely on these features, and careful attention must be paid to the volume of objects represented in our ecosystem. We anticipate a fully decentralized biobanking ecosystem will require multiple classes of NFTs, in addition to fungible tokens, to act as in-game currency. In our proposed solution, we assert that patients do not have to pay as it is their right to transparency over their own donations. Gas fees for on-chain transactions should be rolled into the research budgets of institutional stakeholders as expenses related to patient outreach and community engagement. Importantly, each organoid generated in our local setting requires roughly $1,600 in biobank services, upwards of $1,000 in supplies, in addition to highly specialized labor and equipment for processing and cultivation. Due to the cost, scarcity, and importance of each organoid, as well as the high costs of shipping and handling real-world organic items, transactions are relatively infrequent and high in value. Thus, Ethereum gas fees represent a small fraction of the total cost related to organoid biobanking and must be considered in light of the potential benefits, including cost-savings and increased market value, that may be obtained when patients are engaged.

Next Steps

To address these limitations, a logical next step is to design, develop, and deploy a live pilot study for patients with samples stored in a real biobank repository.[4] A pilot study will require navigation of complex stakeholder relationships across hospitals, universities, and research institutions. Approval from the IRB, informed consent from patients, and collaboration with biobanks offer a valuable opportunity to refine our technical approach as well as our understanding of existing dynamics and stakeholder incentives within a research ecosystem. To advance beyond our proof-of-concept, we must establish the feasibility of our technical solution by integrating it with existing institutional systems, implementing a donor onboarding and verification process that is compliant with IRB policies, and gathering feedback from end users in a live pilot to assess our implementation. Strategies for educating patients about the value of their participation and engagement in organoid research will be critical. Findings from our foundational surveys, interviews, and focus groups with patients regarding engagement in organoid research will be reported elsewhere.

The financial viability and long-term sustainability of an NFT organoid platform will require value propositions, cultural imperatives, and potential policy changes to secure buy-in from all relevant stakeholders.[26] Additional research is exploring how novel market designs, tokenization strategies, and user interfaces may incentivize collaboration, operationalize dynamic consent[27] and decentralized governance, and propose innovative methods for the ethical inclusion of patients in commercialization. Financialized elements of decentralized biobanking will be especially critical to explore relevant in the setting of high-value research products such as organoids, which may cost $4,000 to $7,000 per mL. Each copy of these living cancer models is commercially valuable as precision medicine tools and drug discovery platforms and may be used in countless research studies in many settings over many years. Our initial proof-of-concept prototype demonstrates the potential application of decentralized biobanking technology to organoids as a critical use case. Subsequent research and development activities are addressing feasibility from an economic, market and operational standpoint. Ultimately, the ethical and clinical benefits of keeping patients connected to their organoids is a compelling value proposition for which we believe there will be widespread public support.

Our research and development of decentralized biobanking technology is rooted in the ethical imperatives to improve the efficiency and equity of the biobank research ecosystem. We note that greater transparency, decentralization, and distribution of power through our proposed mechanisms may introduce new challenges for health, safety, and economic implications of organoid technology, and biobanking more broadly. Critically, our ongoing market design research addresses the potential unintended consequences of tokenizing biospecimens and organoids. Our proposed system must be respectful of patients, mindful of potential consequences for research, and equitable in its approach to monetization. Success for decentralized biobanking will require a commercialization model that enhances the effectiveness and speed of creating public-private partnerships for biospecimen research and improving marketplace efficiency and technology advancement. Overcoming the limitations of the current operational regime, which unjustly excludes patients, will be an essential step toward an ethical biospecimen marketplace solution. Ongoing research is exploring the decentralized governance mechanisms, as well as ethical and practical guidelines, that will be required to promote the flourishing of the stakeholders, diversity, and inclusion in our proposed NFT biobank ecosystem.

Conclusion

Decentralized biobanking applies blockchain technology to democratize biomedical research, unlock cures, and promote health equity. Including patients in biobanking, research, and development of organoids is an ultimate use case for de-bi, given the potential for personal significance, clinical impact, and distributive justice across the forefront of the biobank ecosystem. Our proof-of-concept prototype study demonstrates how an NFT-backed framework built on a public blockchain may empower patients as stakeholders in organoid research, enabling dynamic engagement and efficient distribution of images, educational materials, and other rewards of research. A decentralized biobanking mechanism has the potential to reconnect patients to donated biospecimens without compromising privacy, advancing research by forging digital communities and new opportunities for collaboration that are grounded in real-world relationships and modeled on actual biospecimen transactions. The de-bi approach realizes unprecedented respect for patient contributions while ensuring compliance with established de-identification protocols and generating new possibilities for a decentralized biobanking ecosystem. Further research and development are ongoing to ready de-bi technologies for deployment in next-generation organoid research networks.

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Financial and non-Financial Relationships and Activities

The co-authors, Dr. Gross, Ms. Hood, and Mr. Sanchez, have formed de-bi, co., a company focused on the research and development of decentralized biobanking technologies to empower transparency, accountability, and engagement in biomedical research. Co-author, Dr. Miller, has stock options from de-bi, co. and receives payment from the American Society for Radiation Oncology (ASTRO).

Contributors

Mr. Sanchez performed a literature review, reviewed and cleaned the source data, and prepared the first draft. Mr. Linder performed the literature review and supported the development of the first draft. Ms. Hood performed interviews, collected data, and reviewed the manuscript for critical content expertise. Dr. Goss developed the model dataset, was responsible for overall technology design, and closely oversaw prototype development and testing.

Application of AI-Generated Text or Related Technology

No AI-generated text or related technology was used in any study activities or in the preparation of this manuscript.

Data Availability Statement (DAS), Data Sharing, Reproducibility, and Data Repositories

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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