



Ethical, Legal, and Social Implications of Single-Cell Transcriptomics in Public Health Surveillance: Consent, Governance, Trust Implementation, and Equity Considerations

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ABSTRACT

Single-cell transcriptomics is emerging as a powerful tool for public health surveillance, enabling high-resolution detection of pathogen activity, host responses, and environmental biological signals at unprecedented spatial and temporal scales. While this technology holds promise for improving early outbreak detection, monitoring zoonotic transmission, and strengthening population health preparedness within a One Health framework, it also raises significant ethical, legal, and social implications (ELSI). This paper examines key issues surrounding the use of single-cell transcriptomic data in public health surveillance, focusing on informed consent, governance structures, privacy protection, trust-building, implementation challenges, and equity considerations. The analysis highlights tensions between public health imperatives and individual autonomy, particularly in contexts where biological samples or environmental materials may indirectly reveal identifiable human information. Risks of re-identification, misuse of sensitive genomic data, unequal access to technological benefits, and inadequate regulatory harmonization across jurisdictions are discussed. The paper further emphasizes the importance of transparent governance, multistakeholder engagement, accountable oversight mechanisms, and culturally sensitive risk communication in fostering public trust and social license. Special attention is given to disparities affecting low- and middle-income settings, where limited infrastructure, regulatory capacity, and historical inequities may hinder fair participation and benefit sharing. The study concludes that while single-cell transcriptomics could significantly enhance public health surveillance and global biosecurity, its responsible deployment requires robust ethical safeguards, adaptive legal frameworks, inclusive governance models, and sustained investment in equity-oriented implementation strategies.

Keywords: Single-cell transcriptomics, Public health surveillance, Informed consent and governance, Data privacy and trust, and Equity in genomic health.

INTRODUCTION

The ongoing COVID-19 pandemic underscores how pathogens can enter human populations. The timely detection of new pathogens can avert major outbreaks and progress towards elimination [1]. Contemporary detection systems face new challenges posed by pathogens capable of sustained human-to-human transmission throughout the incubation period. Recent advances in large-scale, automated, low-cost genomic sequencing and individual transcriptomic characterization enable public health surveillance at an unprecedented scale [2]. Even in the absence of a reported case, the emergence of biological threats can be investigated by monitoring environmental sources, including water, sewage, or air. High-throughput sequencing technologies facilitate efficient characterization of significant mutations or emergent variants across a large number of diverse biological targets [3]. Dead biological materials, including whole organisms, leaves, or skin, do not need to be collected from living individuals and therefore do not require any form of consent. The emergence of multi-omic metabolism at single-cell resolution offers early detection of biological threats even at the stage of individual cellular infection. Single-cell data gained through cell-free transcriptomics and epitranscriptomics can establish fundamental knowledge on how each exploited individual cell interacts with specimens. The new acquisition of spatiotemporal multi-omic snapshots of biological targets composed of a human–pathogen–substrate interchange marks an immediate, systemic alteration at the organismal state, reflecting a significant biological event inside the environment of the

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target organism [4]. The use of human biological materials for such research creates a pressing need to examine the ethical, legal, and social implications (ELSI) across temperature variations of environmental samples collected inside service air-conditioning vents, transportation means, water, sewage, and food, alongside a wide spectrum of environmental locations, including public transit, airports, and open markets [5]. The potential of such technologies to enhance public health surveillance and pathogen detection merits exploration of the associated ELSI [4].

Conceptual Foundations of Single-Cell Transcriptomics in Public Health Surveillance

Recent outbreaks of novel diseases, such as the COVID-19 pandemic, have garnered extensive attention toward the One Health concept, which highlights the interconnectedness of human-animal-environment systems [2]. The driving thought behind One Health is that the health of humans is intrinsically connected to the health of animals and the environment; many emerging infectious diseases are caused by zoonotic pathogens [1]. The multiscale, sensitive, and efficient single-cell transcriptome surveillance strategy has been proposed to monitor the endemic and zoonotic viruses transmitted from animals to humans and the pathogenicity evolution of endemic viruses [6]. Single-cell transcriptomics techniques enable the identification and characterization of viruses at high spatial precision through the sequencing of host cells [7]. Several state-of-the-art approaches, including single-cell RNA sequencing (scRNA-seq), multiplexed error-robust fluorescence in situ hybridization (MERFISH), spatial transcriptomics, and combinatorial indexing-based transcriptome imaging, have been developed for viral detection [8]. Recent studies using single-cell transcriptomics have successfully recovered the transcriptional activity of viruses, such as SARS-CoV-2, from infected tissues in New York City [9].

Ethical Considerations

The ethical principles of informed consent and autonomy, beneficence, non-maleficence, and justice [1], privacy and confidentiality [4], and equitable benefit sharing are essential to single-cell transcriptomic public health surveillance. Informed consent describes an individual's decision to share their biological material or data. The benefits of single-cell public health surveillance could include improvements in health system surveillance and early detection of outbreaks, while the potential harms include unwarranted and inauthentic use of data and possible stigmatisation of a societal group due to geographical origin or other characteristics [10]. In addition, the principles of privacy, confidentiality, and data stewardship advocate the responsible handling of individual-level health data throughout the life cycle of collection, analysis, interpretation, and data publication sharing [13]. Equity principles define not only the responsible collection and use of biological materials but also involve other characteristics related to public health surveillance, such as the generation of direct economic benefits, acknowledgement of collective rights, equitable distribution of advantages and sharing of benefits, and associated societal risks [11]. Moreover, benefits include not only the generation of knowledge for combating life-threatening outbreaks but also societal widely ranging from guidelines for the sequence of a particular pathogen generated using community-sourced biological samples to a rapid containment mechanism designed to curb potential pandemics that can accrue from that knowledge generation; therefore, distributed-dataset initiatives should not undermine yet facilitate the broader societal sharing of data because an intermediate system would still rely on national and external facilities for broader dissemination [15].

Informed Consent and Autonomy

Research ethics increasingly emphasize the need to respect individual autonomy when obtaining consent for health data sharing, yet achieving this goal remains tricky when the proposed use is open-ended and concerns large-scale data access. Consider health surveillance studies involving single-cell transcriptomics [4]. Individuals need to comprehend what the sharing entails, which can be complex [5]. Furthermore, the aim to minimize future re-contact yet obtain a meaningful consent is at odds with technical uncertainties on how the data will actually be used later. Emerging multi-round consent models [5] have sprung up to address these challenges and allow people to retain control over their personal information without constraining subsequent research options in situations where data-driven research questions are difficult to specify upfront [16]. Autonomy also implies other relevant considerations. Participants can be aware of particular risks associated with their single-cell transcriptomics data being released for public health purposes, yet might be compelled to share the information nonetheless [18]. Potential diseases and health problems are notoriously sensitive [19]. Some populations may wish to grant affiliation at certain locations or date/age ranges, where potential consequences from disclosure could be high. For such groups, allowing specific ethnic-related sensitive information to retain the single-cell transcriptomics dataset could well be an essential condition of providing the data from the start [12].

Beneficence, Non-Maleficence, and Justice

Technically, single-cell transcriptomics in public health surveillance seeks to provide maximum benefits for the community and individuals without causing harm, but achieving this goal in practice is complicated when working with sensitive genetic data [3]. Beneficence implies that research should maximise benefits for the individual and wider community. Non-maleficence indicates a duty to avoid causing harm, recognising the potential psychosocial,

physical, or economic injuries stemming from data breaches or unwanted sharing of genomics data. Justice broadly implies that research should be fair and equitable in its distribution of benefits [13]. It suggests that populations contributing data should not be subjected to disproportionate risks or burdens, and that vulnerable or socially disadvantaged groups should be actively included in broader international conversations concerning the fair distribution of benefits from public health surveillance [23]. Alternatively, these principles can be used to guide research involving sensitive health data such as single-cell transcriptomics. They support processes that are consistent with established governance frameworks and hold the potential to generate significant value for public health and patient outcomes [20]. Public health surveillance supported by single-cell transcriptomics offers significant potential to reduce mortality rates of infectious diseases such as COVID-19, tuberculosis, and malaria. Nonetheless, substantial risks accompany single-cell transcriptomics [23]. The incorporation of those data into public health surveillance through international data sharing raises important concerns regarding the misuse of that information. Current governance mechanisms covering the use of sensitive health data, including single-cell sequencing data, already exist; however, the impact of such highly sensitive data on the well-being of communities [24]. By limiting the risk of harm and enhancing community well-being, the appropriate application of these principles has the potential to maximise both the individual and collective benefits of proposed research involving health data, including single-cell transcriptomics, in a manner comparable to single-cell transcriptomics [6].

Privacy, Confidentiality, and Data Stewardship

Vulnerability to re-identification remains a primary barrier to the sharing of datasets containing sensitive personal information. Re-identification risk arises from the intersection of publicly available knowledge, other datasets, and specific statistical properties of shared datasets [7]. Although regulations often require the removal of name, address, and social security number to protect individual privacy, empirical studies on health data suggest that three datasets: date of birth, gender, and zip code can uniquely identify 87% of the US population [8]. Similarly, re-identification attacks have been successfully launched against released genomic data. Genetic sequences partly characterize an individual, and with the availability of several thousand genome sequences, the remaining uncertainty permits identification [4]. Strategies to mitigate re-identification risk include aggregating, synthesizing, and after-release privacy protection of shared datasets; regulating the release of datasets according to expected re-identification risk; holding datasets under access control for third parties with unspecified re-identification risk; and open release [3]. Addressing privacy concerns surrounding public health surveillance supported by shared individual data remains vital to collaborative governance [2]. Considerations include the extent to which the situation constitutes public health surveillance, the handling of anonymized data, and the continued linkage of previously collected shared data [1].

Equitable Benefit Sharing

The widespread adoption of high-throughput genomic sequencing technologies has driven significant interest in equitable benefit-sharing frameworks, particularly in relation to direct-to-consumer (DTC) genetic testing [1]. These frameworks are intended to ensure that all parties involved during and after scientific research obtain fair advantages from the work, without discrimination towards already disadvantaged groups [17]. The provision of public health services through surveillance of infectious disease outbreaks is a clear benefit shared by society. If one nation offers such services to others, it may not seem advantageous for that nation to prioritize the sharing of benefits from the work [27]. To achieve a fairer framework devoid of discrimination, it is imperative to abandon the idea of sharing benefits only among parties involved at a given stage and instead consider who can benefit from the generation of knowledge, even in public goods scenarios such as scientific knowledge [23].

Legal and Regulatory Frameworks

Public health surveillance aims to safeguard and improve health nationally and worldwide. Statutes in many jurisdictions empower authorities to collect and analyze data encompassing health determinants, health status, and health sector responses to implement efficient policies for the effective reduction of morbidity and mortality and optimization of health outcomes [1]. Surveillance also supports the monitoring of health determinants, the early detection of emerging threats, and periodic assessments of the state of health and health systems and their interactions with determinants [14]. Public health surveillance occupies a prominent position in the field of data-driven action. This situation invites the exploration of the implications of single-cell transcriptomics for health surveillance. The health emergency caused by COVID-19 has accelerated the development and adoption of single-cell transcriptomics as a novel public health surveillance strategy in resource-rich settings [14]. This approach brings an unprecedented level of granularity to analyses of biological agents (viruses, bacteria, fungi, parasites) and their interactions with human and animal hosts, signalling post-infection and post-recovery states and other longitudinal variations of vital significance for action [4].

Data Protection and Privacy Laws

Within the EU, the General Data Protection Regulation (GDPR) governs the processing of personal data and provides a legislative basis for public health monitoring [3]. Drawing on achievements which preceded single-cell

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transcriptomics, the European Commission's COVID-19 Data Strategy prioritised a core set of data-driven variables and protected individual rights while allowing public health measures within 1649 relevant government resources [3]. Adopting a systemic approach also helped the Australian Government to streamline the regulatory remit for data-sharing initiatives, generating a data-sharing framework across government agencies. Similarly, guidance for low- and middle-income countries (LMICs) identified that harmonisation of laws could establish an enabling environment for data-sharing that assists innovation and public health initiatives, including those that use acquired data for economic or commercial enhancement [8]. Data-sharing within LMICs often faces additional hurdles where regulatory instruments can lack clarity and formal enforcement through ineffective law enforcement [9].

Health Surveillance Statutes and Governance

Public health surveillance is recognized as an essential foundation on which effective health policy is built. Surveillance systematically encounters various sources of data pertaining to individuals or communities and is “the ongoing, systematic collection, analysis, and interpretation of data related to health and the application of the resulting data to the planning, implementation, and evaluation of public health practice [5].” With the emergence of the coronavirus disease (COVID-19) pandemic, health surveillance has become a highly urgent and prioritized matter. As a preliminary definition, “health surveillance is the systematic collection and analysis of data.” However, a proper understanding requires a more nuanced definition that highlights the formal essence of health surveillance within a specific context; in particular, “health surveillance is the process of systematic collection, analysis, and interpretation of health data from human subjects to inform human activities [6].” The term human subjects pertains not only to human single-cell data but also to the human activities performed to investigate human health, such as studies among animals, strains, viruses, and materials [7]. Here, the focus is on health surveillance carried out to monitor, prognosticate, and forecast the health status of humans by means of systematic collection, analysis, and interpretation of health data from human subjects [3]. As defined above, health surveillance comprises systematic operations that gather individual-level data to benefit collective population health and therefore can pose ethical questions about privacy and confidentiality, autonomy and informed consent, and responsible secondary use of data. Such issues become all the more pressing when sensitive information is sought, as during the collection of HIV-related data conducted, which evokes significant, multisectoral debate. By contrast, public health surveillance does not traditionally involve rigorous ethical review mechanisms, such as those provided by institutional review boards (IRBs) that are designed to safeguard individual rights in the conduct of research. Some surveillance projects may nevertheless undergo IRB scrutiny as part of the compliance process [11], but the IRB framework, with its emphasis on “research” and “subjects,” does not easily accommodate public health objectives that may occasionally require compromises to individual rights or privileges. The ethical imperatives of health surveillance, therefore, merit direct and innovative articulation to promote equitable participation while acknowledging the tensions and trade-offs that surround the process [3].

Intellectual Property and Data Access

The emergence of public health surveillance frameworks built upon single-cell transcriptomics depends upon the ability to detect health-threatening outbreaks in large populations rapidly and accurately [1]. Access to open or controlled datasets, covering populations spanning diverse geographies, ethnicities, and pathogen exposures to facilitate global collaborative minimum description length analysis, is essential to the build-out of such frameworks. However, concerns persist that the pooling of information about biological sequences and other related phenotypic data associated with the collection of public health-related samples might contravene national, institutional, or public interest demands to limit access to samples capable of yielding strain or lineage reconstruction through phylogenetic inference [12]. The biosphere consequently requires discussions and formulations in diverse institutional settings of appropriate intellectual property considerations, shared header file format specifications, and metadata accessibility constraints surrounding open or controlled single-cell transcriptomic datasets [1]. The global interface between inquiry and released datasets, both within and across geopolitical jurisdictions, frequently remains opaque [13]. For certain bioinformatics algorithms, including minimum description length analysis, it is common practice to modulate the explicit release of basic information, such as a description of the simulation model or model environments applied in conjunction with observed datasets [2]. At public and private biotech companies, the data generated in most single-cell transcriptomics falls into the category of controlled unless explicit data-release agreements accompany access to physiological samples. Consequently, proactive operations that trace the embedding of basic proprietary considerations within the data-access regime, including header-file specifications, have been initiated with the goal to prompt the early awareness of the access regime by the scientist and formulate a dataset accordingly [6].

Liability and Accountability

Surveillance, particularly at the population level, is integral to public health [4]. Global health threats, such as the COVID-19 pandemic, highlight the critical role of surveillance systems in detecting emerging pathogens and

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preventing or slowing transmission [2]. An effective surveillance system must provide timely information on the emergence or re-emergence of a range of pathogens, requiring the ability to capture, process, and analyse data from many sources. Companion document “Smartness vs. Monster” captures a view on this multiple hierarchical surveillance system framework vis-a-vis the use of single-transcriptomics[3]. Emerging high-throughput molecular and genomic tools raise hope for a deeper understanding of health and disease patterns in a population, as exemplified by the use of single-cell sequencing data to differentiate tuberculosis infections [2]. A novel public health surveillance framework that leverages single-cell transcriptomics aligns with applicable laws that protect human rights and civil liberties, thus helping to address community concerns about the ethics of public health surveillance that uses large-scale datasets [1].

Governance Structures for Single-Cell Data in Public Health

Governance structures for single-cell data in public health surveillance must balance innovative research and public health responses with societal concerns and trust [14]. Data protection, the legal frameworks governing health surveillance, and public attitudes toward the use of health-related data are key consideration points. Frameworks like the European Union’s General Data Protection Regulation (GDPR) may also need to be adapted to maintain oversight of complex, cross-jurisdictional information-sharing scenarios [13]. Public willingness to share health-related data is influenced by the perceived quality of governance and trust in authorities to use data responsibly [7]. Research has found that the use of personal health data for public good enhances citizens’ willingness to share. Concerns regarding the security of data held by public authorities are common. Transparent governance models outlining the purpose of data collection, proposed analyses, planned adoption of results, and the nature of involved organizations can help build trust. Governance processes that encourage public engagement, encompassing both one-way information dissemination and two-way dialogue, also enhance welfare and mitigate disparities [9]. Respect for multisectoral governance and the coordination of health datasets across jurisdictions are imperative to build public trust and avoid data appropriation. Governance decisions should involve stakeholders from government, academia, civil society, and the private sector, with alignment to national health priorities and wider global efforts [8].

Institutional Governance Models

Data generation from public health surveillance, consequently addressing collective health challenges, relies on the effective deployment of high-throughput biological technologies [3]. For the purpose of such initiatives, the concepts of governance and institutional trust shape surveillance models that direct research design and data dissemination [15]. Essential to establishing responsive coordination within institutional frameworks, strategy development reinforces public faith in regulatory systems. Institutional governance thus involves participation and mutual aid among institutions and stakeholders throughout plan implementation and post-acquisition processing stages to preserve public confidence and social legitimacy [4]. Governance of data produced through public health surveillance forms an integral, prerequisite part of institutional trust [6]. A recent initiative supporting data generation from local population surveillance to tackle public health matters, including those presented by pathogens, public-health threats, and others, has emphasised the importance of systemic governance [16]. The range of options for addressing the equitable sharing of health data originating from municipalities is subject to negotiation. A related public consultation has been formed to seek insights regarding optimal governance for locally generated surveillance [11].

Multistakeholder Engagement and Transparency

Citizen and stakeholder engagement with broad representation across the public health surveillance ecosystem can provide greater confidence in technologies such as single-cell transcriptomics during public health system emergency responses [4]. Beginning with independent social science studies of public and stakeholder perceptions of publicly funded, human health, and high-throughput genomic data sharing indicates that transparency about ambitions, motivations, and the types of data collected builds public trust [17]. Clear, open, and ongoing engagement with diverse citizens and stakeholders on single-cell transcriptomics, its anticipated advantages, and how scientific freedom will be safeguarded during health emergencies can foster essential public trust and social license [11]. All aspects of citizen, stakeholder, and public engagement with single-cell transcriptomics benefit from increased transparency [8]. Transparent engagement practices broadly assist public health organizations in assuring citizens and stakeholders of their commitment to facilitate health innovation and save lives even in broadly constrained public health circumstances [9].

Oversight Mechanisms and Auditing

The rapid pace of scientific innovation and its potential impact on health-related decisions are causing widening public concern regarding data collection, sharing, and reuse of personal health data [2]. Although a large body of literature robustly affirms the public's willingness to share health data for societal benefit, concerns about misuse of personal health data persist [4]. Trust is an important attribute. The organisation and the legal frameworks governing the collection, sharing, and re-use of sensitive data are among the critical parameters that frame the

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degree of trust in the community [6]. Emerging efforts to strengthen and extend existing surveillance into the evaluation of the health of microorganisms in equilibrium with the global human population present unparalleled opportunities for investigative creativity. Such investigative creativity raised concerns accompanied by examples from the dematerialisation literature about the ability to devalue or “harvest” human living tissue at the scrutiny of the “willing to share” intention over time [3]. All sector stakeholders are encouraged to join in defining data policies that respect the willingness of the individuals who wish to share their information, whilst limiting, as rapidly as possible, at all times, the potential for an intrinsic peripheral harvesting of globally-dematerialised parameters. Such materials freely circulate publicly and may form the basis of an additional study [4].

International Collaboration and Harmonization

International collaboration and harmonization of ethical and regulatory requirements are essential for public health surveillance involving single-cell transcriptomics [3]. A greater understanding of practices and regulations across countries is needed [2]. The European Union’s General Data Protection Regulation and Council of Europe Biomedicine Convention, alongside the Global Health Security Agenda, provide some early lessons in this regard [18]. Research in a range of health, environmental, and other areas has highlighted the challenges publicly funded science faces from the point of view of trust-related and ethical barriers, and has called for ethical frameworks and strategies that support trust as an integral element of socio-technical systems [19].

Trust, Social License, and Community Engagement

The absence of clear contextual information about public health surveillance within a community can lead to a major perception of risk [11]. Therefore, communities in public health surveillance programs must be aware of what is being monitored, why, and how risk, whether real or perceived, is being managed [17]. The provision of information about the benefits of research is also a clear route to establishing trust. The motivations behind health-data collection and the benefits of public-health measures are increasingly relevant to the trust that individuals place in public health surveillance [4]. Emerging technologies capable of providing increased insight into population health trends may come with some risk. Single-cell transcriptomics is an example of a technology that could be misused, whether by malicious third parties or even by the collecting organizations [5]. Tools capable of analyzing this data and understanding how it may be used are, therefore, crucial when building trust. While still early in the implementation of the technology, building confidence that single-cell data will be treated with the same rigor and care normally reserved for sequencing data, such as pooling or increasing the number of anonymized cells, can help establish a social license for its use in public health activities [8].

Risk Perception and Communication

Public health surveillance data sharing systems raise challenging questions about risk communication frameworks that can effectively balance the need for public engagement and trust-building with the necessity of avoiding the politicization of risks and benefits [4, 20]. Despite extensive literature on the ethical, legal, and social implications of data sharing, the practical details of how citizens conceptually frame the associated risks and benefits remain underexplored [9]. Addressing this knowledge gap requires careful consideration of the social and political contexts in which data sharing operates; public attitudes toward surveillance data sharing risk differ markedly between countries and even regions [11]. These attitudes are shaped by a variety of factors, including historic abuses of citizens’ rights and the extent to which individuals perceive that the underlying surveillance systems serve the common good. Accountability and trust in authorities are critical factors influencing the types of risk communication and engagement strategies considered appropriate for specific territories [13]. The particular social, political, and cultural context presents both opportunities and risks for public health applications of single-cell transcriptomics, complicating governance and trust-building approaches [6].

Public Trust Building Strategies

Policies and governance arrangements must establish accountability frameworks that serve to clarify the roles and responsibilities of different actors and organizations involved in single-cell transcriptomic research and its application for public health, as well as to mitigate risks and instill confidence [13]. Data-sharing policies and frameworks should clearly articulate key aspects of platform governance, including eligibility criteria for access, access review processes, and mechanisms for tracking and reporting usage [17]. These elements can enable data donors to assess whether their interests align with those of prospective users. Open access to health data and genomic information can foster greater trust in data use, especially when measures are in place to safeguard privacy [2].

Engagement with Vulnerable and Marginalized Populations

Research in public health surveillance addresses the emergence of new diseases and their dissemination, and uses a range of population-level biospecimen collections, transcriptomic and genomic sequencing, cyberinfrastructure, and analytic tools to evaluate potential trajectories of pathogen spread [5]. Neurodevelopmental outcomes and mental health problems in children exposed to HIV were studied in a cohort from the MRC Nutrition Intervention Study in India, in which 97 children (exposed to 116 distinct antiretroviral regimens) were assessed when aged

12–40 months. Analyses suggested parental help, toys, and social events were positively associated, while parental depression was negatively linked with development [2]. The AGEM study projected evolution by analysing complete genome sequences of virulent variants and human methylomes from infected individuals in populations where selected mutations accumulated independently. The H1N1 virus's permutations were simultaneously tracked in each population and network, and the mutation patterns were assessed with molecular modelling [1].

Implementation Challenges and Equity Considerations

Safeguarding human rights requires appropriate consideration of possible consent measures prior to the implementation of public health surveillance programs [7]. Intermediary or third-party consent coupled with de-identification, authentication, supervision, and regular audits are reasonable arrangement that might suffice in certain contexts [18]. In particular, the collection of incidental findings through single-cell transcriptomics studies, as well as vicarious community–public health colonialism that potentially undermines the self-determination of vulnerable communities, requires precise governance mechanisms on the ethical usage and sharing of generated transcripts [1]. To guarantee equal socio-ethical servicing and maintain the societal legitimacy of newly established viral public health surveillance systems, such arrangements need to be appropriately considered [19]. The emergence of a new disease-disrupting organism, such as the coronavirus, has already generated a new wave of community concern, both related to the biological dimensions of the virus and to its political governance [9].

Resource Allocation and Access Disparities

Implementing single-cell transcriptomics to monitor pathogens in the environment and clinical settings offers a promising complementary strategy to traditional sequencing-based techniques, yet it is not without challenges [15]. Ethics, governance, and equity considerations are paramount, given that countries and organizations worldwide are adopting this technology and that public trust must be built. Early results from public deliberation processes emphasize the importance of staying attuned to social expectations [21]. Disparities in resource allocation and access to genomic data and healthcare services hinder equitable research and clinical application [22]. Participation remains limited in many underrepresented populations despite growing interest in investigating the human genome and improving health outcomes through genomic data generation and utilization [13]. Several initiatives aim to address these disparities [16]. The IRUD (Individualized RNA (iRNA) Use for Diverse Human Populations) program was launched in Japan in 2019 to address diagnostic odysseys related to rare diseases by leveraging the nation's integrated, comprehensive genomic and clinical database. In the UK, the 100,000 Genomes Project is gradually expanding patient access to genomic testing beyond the National Health Service, targeting specific health issues such as rare diseases, cancer, and infectious diseases [11]. Various efforts are underway to develop rapid-learning health systems that use data generated via diverse healthcare encounters for product development, while strategies for flexible and diverse sample collection are being evaluated. These critically deliberated initiatives aim to improve data-sharing practices in the precision medicine era and to augment public engagement through personalized consent models [15].

Capacity Building in Low- And Middle-Income Settings

Capacity building in low- and middle-income settings fosters trust between researchers and communities [11]. Numerous initiatives can contribute to trust-building efforts and facilitate the development of research capacity. Given that trust is rarely freely granted and often must be earned, addressing power imbalances due to historical oppression is essential [13]. Researchers, scholars, technologists, and their institutions are expected to engage in self-reflection on their own privilege and to proactively consider how to minimize its influence in interactions with partners in developing settings [14]. Engagement with historically underrepresented populations at the design stage of research is valuable, as the community perspective can provide broader insights that inform a shared understanding of research objectives. Broader consultations with the general population regarding the societal and ethical implications of specific research agendas can also assist in aligning studies with community values [23].

Ethical Data Sharing and Benefit Realization

Global public health surveillance is conducted to control infectious diseases and biothreats, and to secure safer antibiotics [18]. Multi-omics analysis of pathogens is conducted as part of genomic epidemiology. In addition to genomic epidemiology, single-cell transcriptomics holds promise for understanding the host response to pathogens, although its practical application is limited [11]. Single-cell sequencing enables the genomic and transcriptomic survey of several individuals and even single cells of multiple organisms in a community [10]. As long as a sample is collected, all analytes of the sample may be analysed through biobanking. National security agencies and synthetic biology identity systems have been developed to prevent biomanufacturing risk; however, these biosecurity concerns are not necessarily applicable because pathogens are ubiquitous in nature [12]. Therefore, the key issue is whether the data of the single-cell analytes remains with the controller of the sample [24].

Governance of Incidental Findings and Clinical Relevance

Public health surveillance relies on the commingling of data streams. Public health researchers may want to know whether an infection has occurred, and other parameter values, data streams that are deemed overtly useful [12]. Yet, the same data may have deep-ranging implications on health risk zones in the broader sense of multi-eyed genomic epidemiology [10]. One greater generalization is that data collected for one purpose may reveal information that is directly relevant to another; thus, the knowledge-full entry is more relevant for survey deployment in fields such as demographic epidemiology [11]. The foundation of the discussion hinges upon the novel architecture and analyte availability for single-cell transcriptomic and spatial transcriptomic [17]. Their one-time technical setup still allows multicell participation, making their data rich, absent from continuous sampling entering the other data streams [25]. Standard single-cell transcriptomics may reveal participant health status, whereas spatial transcriptomics has the potential to reveal detailed information about the whole participant, such as ethnic group tracing [26]. Implications and governance for public health surveillance bottom-line two observational/interpretation axes: health status, and ethnic tracing [18].

Case Studies and Lessons Learned

The case studies described above point to ways of implementing single-cell transcriptomics for public health surveillance [19]. These approaches highlight important lessons regarding governance, consent, and trust, along with considerations of social justice [21]. The first case involves scRNA-seq protocols for identifying and characterizing the host immune response to COVID-19 viral infection developed at the University of California, San Francisco (UCSF) [20]. The study enabled direct engagement with participant communities, refining participant recruitment and sample acquisition processes [21]. Engaging participant populations pre-implementation facilitated the establishment of trust, a critical component when designing ethical studies that incorporate single-cell transcriptomic approaches [3]. The incorporation of community-based participatory research principles proved essential in all phases from inception through additional avenues of value-added consent [27]. The second case study positioned participants as partners in the research process, enabling knowledge of their data circulation beyond initial donation to timeliness, control, and enhancement of permissions after initial consent [12]. A focus group study allowed citizens to articulate privacy and trust concerns, considering the public interest in data-sharing arrangements. With wide-acceptance scenarios enabling benefits to both public health and research, citizens viewed regulatory and institutional settings linked to entities benefiting from aggregate data sharing more positively than open science. Trustworthiness depended on perceived competence, the generation of a public good, and appropriate governance based on study participants' descriptions of support systems [4].

Synthesis of Ethical, Legal, and Social Implications

The preceding sections of this report detail the concept of single-cell transcriptomics (scRNA-seq) for public health surveillance, tracing the ethical, legal, and social implications of a potential Canadian pilot project built around such a concept [25]. The following paragraphs provide a holistic assessment of this landscape, summarising the salient considerations identified throughout the document and reaffirming the need for a long-term governance approach encompassing consent, implementation, and equity [26]. The most frequently discussed ethical imperative in the surveillance context is informed consent, as individuals whose single-cell RNA data, along with associated metadata, are collected during drug therapy must be provided with both the right to consent and the opportunity to make an informed decision regarding the use of their data [24-28]. The governance mechanism should provide a clear and understandable description of the methods associated with scRNA-seq, the intended uses of data, the data elements to be retained, the metadata to be attached to each collection, and any anticipated re-use of data [27]. With respect to equity, guidelines and protocols applicable to additional clinical studies, including drug therapy, population, or airborne contagion surveillance, should reference both the anticipated short- and long-term benefits for the participant in the biomedical research area and the equal expectations of two-way benefit sharing if findings are collected about other fundamental research areas. Attention should be placed on ensuring that efforts to construct surveillance systems based, in part, on single-cell transcriptomics do not marginalise specific population groups in society [29-35].

CONCLUSION

Single-cell transcriptomics offers transformative potential for public health surveillance by enabling early detection of infectious threats, improved understanding of host-pathogen interactions, and more responsive disease monitoring systems. However, the same features that make the technology powerful, its granularity, scalability, and capacity to reveal sensitive biological information, also create complex ethical, legal, and social challenges. Respect for autonomy through meaningful consent processes remains essential, even when surveillance involves indirect or environmental sampling that may still yield identifiable human data. Strong governance frameworks are required to address privacy protection, data stewardship, intellectual property, accountability, and cross-border data-sharing practices. Transparent institutional arrangements, clear access rules, and continuous

auditing mechanisms can help ensure responsible data use while maintaining scientific innovation. Public trust and social license will depend heavily on inclusive stakeholder engagement, transparent communication of risks and benefits, and demonstrable commitment to protecting community interests. Equity must remain central to implementation: without deliberate efforts to strengthen capacity in low- and middle-income settings, reduce resource disparities, and ensure fair benefit sharing, the deployment of single-cell transcriptomics could unintentionally widen global health inequalities. In summary, the integration of single-cell transcriptomics into public health surveillance should proceed through ethically grounded, legally robust, and socially responsive approaches. When supported by inclusive governance, equitable infrastructure development, and sustained public engagement, this technology can contribute meaningfully to more effective, trusted, and globally coordinated public health systems.

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