Perspectives and directions of biobanking in case of rare types of cancer

E.V. Petersen [1], D.A. Chudakova [1], A.A. Shiryaev [1,2], A.M. Khrushchova [3], E.Y. Shabalina [1], A.A.S. Shaker [1], T.A. Chernov [1], P.A. Karalkin [1,2], I.V. Reshetov [1,2]

[1]Moscow Institute of Physics and Technology, Moscow, Russia
[2]I.M. Sechenov First Moscow State Medical University, Moscow, Russia
[3]A.N. Severtsov Institute of Ecology and Evolution, Russian Academy of Sciences, Moscow, Russia
Contacts: Petersen Elena Vladimirovna – e-mail: Petersen.ev@mipt.ru

Перспективы и направления биобанкирования при редких видах рака

Е.В. Петерсен [1], Д.А. Чудакова [1], А.А. Ширяев [1,2], А.М. Хрущова [3], Е.Ю. Шабалина [1], А.А.С. Шакер [1], Т.А. Чернов [1], П.А. Каралкин [1,2], И.В. Решетов [1,2]

[1]Московский физико-технический институт, Москва, Россия
[2]Первый Московский государственный медицинский университет имени И.М. Сеченова, Москва, Россия
[3]Институт проблем экологии и эволюции имени А. Н. Северцова, Москва, Россия
Контакты: Петерсен Елена Владимировна – e-mail: Petersen.ev@mipt.ru

罕见癌症病例中生物银行的前景和方向

E.V. Petersen [1], D.A. Chudakova [1], A.A. Shiryaev [1,2], A.M. Khrushchova [3], E.Y. Shabalina 1, A.A.S. Shaker [1], T.A. Chernov [1], P.A. Karalkin [1,2], I.V. Reshetov [1,2]

[1]Moscow Institute of Physics and Technology, Moscow, Russia
[2]I.M. Sechenov First Moscow State Medical University, Moscow, Russia
[3]A.N. Severtsov Institute of Ecology and Evolution, Russian Academy of Sciences, Moscow, Russia
Contacts: Petersen Elena — e–mail: Petersen.ev@mipt.ru

Doi: 10.25792/HN.2022.10.4.41–48

Biobanking is an actively developing area of biotechnology and biomedicine. Briefly, Biobank is a comprehensively characterised biological material collected and stored by standardized methods and accompanied by detailed corresponding information, potentially available to many users. Modern biobanks are instrumental for development of new diagnostic and therapeutic approaches, drug development, personalized medicine and many aspects of pre-clinical research. In part, this is because biobanks are not only «places of sample storage», but also places for conducting research using collections of biomedical materials and all associated data, as well as teaching/learning hubs providing methodology training and guidance with experiment design to biobank's clients (and here we emphasize the importance of the human resources component of biobanks – researchers and their unique expertise in biobanking, as an integral part of biobank). Biobanking makes possible to perform various "omics" studies, such as genomics, epigenomics, transcriptomics, proteomics, lipidomics, metabolomics, microbiomics and other "omics" data, and combine them with data obtained on complex 3D tissue culture models, ex-vivo cultures, "patient-like" organoids and "avatars", data obtained from medical image biobanks, radiology biobanks, and others. Such studies can be longitudinal, recruit participants from several geographical regions and of different ethnicity, involve big data analysis using artificial intelligence, include both ante mortem and post mortem samples, samples collected at different time points of chemo- and/or radio-therapy, et cetera.

This review briefly describes the current state of biobanking and discusses the role of biobanks in the study of malignant neoplasms, with particular focus on the rare or poorly differentiated types of cancer (RPDC) and cancers of unkcnown primary (CUP). Unlike well-described types of cancer with known primary, there are cases of CUP when the primary sites of the appearance of cancer cells are not known, of them up to 25 percent are poorly differentiated, which significantly complicates histological typing of the tumor and selection of adequate therapy. Historically, poorly differentiated cancers have been excluded from many biospecimen collections. Rare cancers are malignant neoplasms with very low incidence, but despite low incidence they account to approximately 25 percent of all diagnosed cancers. There is a plethora of rare cancer types among Head and Neck cancers (HNC). In case of rare cancers, paucity of samples and sample-associated data, as well as slow accrual of the samples (so called "sample bottlenecks") create significant drawbacks for translational oncologists. As a result, there are still significant inequalities in healthcare in case of RPDC/CUPs compared to common cancers, such as diagnosis uncertainty, limited therapies, drawbacks in the identification of novel therapeutic targets, and finally difficulties

in conducting pre-clinical research and clinical trials, resulting in a survival gap between common cancers and RPDCs. Therefore, addressing these challenges is of utmost importance. Noteworthy, although rare subgroups of common cancers are not classified as rare cancers, patients belonging to such subgroups might face challenges similar to those affected by the rare cancers. Creating Rare and Poorly Differentiated Cancer Biobanks (RPDCB) and merging single biobanks into big consortia, as well as long-term sample collection in RPDCB, creates unique opportunity to use biobanking to study such diseases and can significantly facilitate research on their etiology and pathogenesis, drug development and therapy development, including personalized, targeted, and per-emptive therapies. In conclusion, there is an unmet need for creation of RPDCBs which should be addressed.
Key words: biobank, biobanking, head and neck cancer, malignant tumors, translational medicine, personalized medicine, oncology, extracellular matrix, 3D cell culture models

Conflicts of interest. The authors have no conflicts of interest to declare.
Acknowledgements. This study was made possible through the support of the Applied Genetics Resource Facility of MIPT (Support Grant 075-15-2021-684)
Funding. Supported by grants №18-15-00391-п, №21-15-00411.
For citation: Petersen E.V., Chudakova D.A., Shiryaev A.A., Khrushchova A.M., Shabalina E.Y., Shaker A.A.S., Chernov T.A., Karalkin P.A., Reshetov I.V. Perspectives and directions of biobanking in case of rare types of cancer. Head and neck. Russian Journal. 2022;10(4):41–48
The authors are responsible for the originality of the data presented and the possibility of publishing illustrative material – tables, drawings, photographs of patients.

Биобанкирование – это активно развивающаяся область биотехнологии и биомедицины. Вкратце, биобанк – это всесторонне охарактеризованный биологический материал, собранный и сохраненный стандартизированными методами и сопровождаемый подробной соответствующей информацией, потенциально доступной многим пользователям. Современные биобанки играют важную роль в разработке новых диагностических и терапевтических подходов, разработке лекарственных препаратов, персонализированной медицине и многих аспектах доклинических исследований. Отчасти это объясняется тем, что биобанки – это не только “места хранения образцов”, но и места для проведения исследований с использованием коллекций биомедицинских материалов и всех связанных с ними данных, а также центры преподавания/обучения, предоставляющие клиентам биобанка методическую подготовку и руководство по разработке экспериментов (и здесь мы подчеркиваем важность кадрового компонента биобанков – исследователей и их уникального опыта в области биобанкирования, как неотъемлемой части биобанка). Биобанкирование позволяет проводить различные “омические” исследования, такие как геномика, эпигеномика, транскриптомика, протеомика, липидомика, метаболомика, микробиомика и другие “омические” данные, и объединять их с данными, полученными на сложных 3D моделях культур тканей, культурах ex-vivo, “пациентоподобных” органоидах и “аватарах”, данных, полученных из биобанков медицинских изображений, радиологических биобанков и др. Такие исследования могут быть продолжительными по времени, набирать участников из нескольких географических регионов и разной этнической принадлежности, включать анализ больших данных с использованием искусственного интеллекта, включать как прижизненные, так и посмертные образцы, образцы, собранные в разные временные точки химио- и/или радиотерапии, и т.д.
В данном обзоре кратко описывается современное состояние биобанков и обсуждается роль биобанков в изучении злокачественных новообразований, особое внимание уделяется редким или плохо дифференцированным типам рака (РПДР) и раку с неизвестным первичным очагом (РНПО). В отличие от хорошо описанных типов рака с известной первичностью, при РНПО встречаются случаи, когда первичные очаги появления раковых клеток неизвестны, из них до 25 процентов являются низкодифференцированными, что значительно затрудняет гистологическую типизацию опухоли и подбор адекватной терапии. Исторически сложилось так, что плохо дифференцированные раковые опухоли исключались из многих коллекций биообразцов. Редкие виды рака – это злокачественные новообразования с очень низкой частотой встречаемости, но, несмотря на низкую частоту, они составляют около 25 процентов от всех диагностированных видов рака. Среди рака головы и шеи (РГШ) существует множество редких видов рака. В случае редких видов рака нехватка образцов и данных, связанных с образцами, а также медленное накопление образцов (так называемые “узкие места”) создают значительные трудности для трансляционных онкологов. В результате в здравоохранении все еще существуют значительные неравенства в случае РПДР/РНПО по сравнению с обычными раками, такие как неопределенность диагноза, ограниченность методов лечения, недостатки в определении новых терапевтических мишеней, и, наконец, трудности в проведении доклинических исследо-

ваний и клинических испытаний, что приводит к разнице в выживаемости между обычными раками и РПДР. Поэтому решение этих проблем имеет первостепенное значение. Примечательно, что хотя редкие подгруппы распространенных видов рака не классифицируются как редкие раки, пациенты, принадлежащие к таким подгруппам, могут сталкиваться с проблемами, аналогичными тем, которые возникают при редких видах рака. Создание биобанков редких и плохо дифференцированных раков (РПДРБ) и объединение отдельных биобанков в крупные консорциумы, а также долгосрочный сбор образцов в РПДРБ создает уникальную возможность использования биобанков для изучения таких заболеваний и может значительно облегчить исследования их этиологии и патогенеза, разработку лекарств и терапии, включая персонализированные, целевые и упреждающие методы лечения. В заключение следует отметить, что существует неудовлетворенная потребность в создании РПДРБ, которую необходимо удовлетворить.

Ключевые слова: биобанк, биобанкирование, рак головы и шеи, злокачественные опухоли, трансляционная медицина, персонализированная медицина, онкология, внеклеточный матрикс, 3D модели клеточных культур

Конфликты интересов. У авторов нет конфликтов интересов, о которых они могли бы заявить.
Благодарности. Данное исследование стало возможным благодаря поддержке Ресурсного центра Прикладной Генетики МФТИ (грант поддержки 075-15-2021-684).
Финансирование. Финансирование. Поддержано грантами №18-15-00391-п, №21-15-00411.
Для цитирования: Петерсен Е.В., Чудакова Д.А., Ширяев А.А., Хрущова А.М., Шабалина Е.Ю., Шакер А.А.С., Чернов Т.А., Каралкин П.А., Решетов И.В. Перспективы и направления биобанкирования при редких видах рака. Голова и шея. Российский журнал. 2022;10(4):41–48

生物银行是生物技术和生物医学的一个积极发展的领域。简而言之，生物库是通过标准化方法收集和存储的具有全面特征的生物材料，并附有详细的相应信息，可能供许多用户使用。现代生物库有助于开发新的诊断和治疗方法，药物开发，个性化医疗和临床前研究的许多方面。部分原因是，这是因为生物样本库不仅是“样本存储场所”，而且是利用生物医学材料和所有相关数据收集进行研究的场所，以及为生物库客户提供实验设计方法培训和指导的教学/学习中心（在这里，我们强调生物库中人力资源组成部分的重要性–研究人员及其在生物库中的独特专业知识，作为生物库的组成部分）。生物银行可以进行各种“组学”研究，如基因组学，表观基因组学，转录组学，蛋白质组学，脂质组学，代谢组学，微生物组学和其他“组学”数据，并将它们与复杂3D组织培养模型，离体培养，“患者样”类器官和“化身”，从医学图像生物库，放射学生物库获得的数据，和其他人。这些研究可以是纵向的，招募来自几个地理区域和不同种族的参与者，涉及使用人工智能的大数据分析，包括宰前和死后样本，在化学和/或放射治疗的不同时间点收集的样本，等等。

本综述简要介绍了生物银行的现状，并讨论了生物银行在恶性肿瘤研究中的作用，特别关注罕见或低分化类型的癌症（RPDC）和未知原发性癌症（CUP）。与已知原发性癌症的描述类型不同，当癌细胞出现的主要部位未知时，存在CUP病例，其中高达25%的分化差，这显着复杂化了肿瘤的组织学分型和选择适当的治疗。从历史上看，低分化癌症已被排除在许多生物样本集合之外。罕见癌症是发病率非常低的恶性肿瘤，但尽管发病率很低，但它们约占所有诊断癌症的25%。头颈癌（HNC）中有许多罕见的癌症类型。在罕见癌症的情况下，样本和样本相关数据的缺乏以及样本的缓慢累积（所谓的“样本瓶颈”）给转化肿瘤学家带来了重大缺陷。因此，与常见癌症相比，RPDC/CUP的医疗保健仍然存在显着的不平等，例如诊断不确定性，有限的治疗方法，确定新的治疗靶点的缺点，以及最终难以进行临床前研究和临床试验，导致常见癌症和RPDC之间的生存差距。因此，应对这些挑战至关重要。值得注意的是，尽管罕见的常见癌症亚组未归类为罕见癌症，但属于此类亚组的患者可能面临与罕见癌症相似的挑战。创建稀有和低分化的癌症生物库（RPDCB），并将单个生物库合并为大型财团，以及RPDCB中的长期样本收集，为使用生物库研究此类疾病创造了独特的机会，并可以显着促进对其病因和发病机理的研究，药物开发和治疗开发，包括个性化，针对性，和每个先发制人的疗法。总之，创建RPDCB的需求尚未得到满足，应予以解决。

关键词：生物库，生物库，头颈癌，恶性肿瘤，转化医学，个性化医学，肿瘤学，细胞外基质，3D细胞培养模型

利益冲突：作者没有利益冲突要声明。
致谢：这项研究是通过MIPT应用遗传学资源设施（支持补助金075–15–2021–684）的支持而实现的
基金：融资。 由第18–15–00391–p、第21–15–00411号拨款资助）。
引用: **Petersen E.V., Chudakova D.A., Shiryaev A.A., Khrushchova A.M., Shabalina E.Y., Shaker A.A.S., Chernov T.A., Karalkin P.A., Reshetov I.V. Perspectives and directions of biobanking in case of rare types of cancer. Head and neck. Russian Journal. 2022;10(4):41–48**

Introduction

Over the course of the last couple of decades, biobanks have become one of the crucial tools in biomedical research, including translational oncology. In the modern sense of the term, a biobank is a structure that includes collections of samples of biological materials (such as tissues, biological fluids, and others), medical and biological images (for example, MRI, PET scan, microscopy images), other relevant data, as well as a descriptive database corresponding to the samples. Descriptive database can be of a clinical and sociology-demographic nature, include information about methods of collecting, processing and storing of the samples, their geographical origin, and any other relevant information. Biobanks comply with the standard ISO 20387 and, in Russian Federation, GOST R ISO 20387-2021. Such standardization of biobanking allows merging data and results from multiple independent interdisciplinary studies as well as creating biobanks consortia. All of this distinguishes biobanks from conventional scientific and/or medical collections, increases precision of the studies based on their resources, makes biobanks a valuable tool for development of new therapies, diagnostic and prognostic markers, as well as novel methodological approaches in translational medicine. Biobanks are also instrumental for optimization of the standard practical tasks in medicine (organ and tissue transplantation, reproduction medicine) [1]. The ideal scenario for biobanking assumes that its collections will be utilized to solve a wide range of interdisciplinary problems using many different technologies, by independent teams of researchers with different scientific aims and expertise, during long time period.

According to the standard ISO 20387 developed by the International Organization for Standardization (ISO), biobanking is “the process of collecting and storing, as well as some or all of the following: collection, preparation, storage, testing, analysis and dissemination of biological material, as well as related information and data”. It is also expected that biobanks strictly adhere to all relevant legal and ethical standards [2].

Biobanks in medical research are traditionally divided into populational and nosological ones, and the latter are sub-divided into non-specialised or general biobanks (for example, biobanks of any types of malignant tumors) and specialized ones (for example, collections of a certain types of rare cancer). By the size and localisation, biobanks are classified into local, regional, state, international biobanks, as well as global networks of biobanks [3]. Biobanks already have proven to be instrumental to study common cancers.

As mentioned above, biobanks include not only biological samples and related information, but also so-called “material and technical base” (equipment, software, facilities, etc) necessary to replenish, maintain, and characterize the collection. Appropriately qualified personnel with experience and expertise in this particular area is also a key component of a biobank [4]. Thus, standardisation should be extended not only to the methods of collecting, validating and storing biosamples, but also to all other relevant standard operating procedures in biobanking, including collecting and storing related information, as well as to procedures of the personnel training [5].

There are several excellent reviews about problems and achievements of contemporary biobanking published already ((6-9), and others), thus to avoid redundancy in our review we will focus solely on the most recent milestones in the biobanking of HNC or RPDC/CUPs, and also propose and discuss possible methodological approaches and practical applications of biobanking not outlined elsewhere in details.

Cancer biobanks consortia

Aforementioned, as a result of the combining several biobanks into a single consortium it becomes possible to reach a new level of translational research, including interdisciplinary research in translational medicine and translational oncology. Biobank consortia exist worldwide, in a number of countries, for example the International Head and Neck Cancer Epidemiology consortium (https://medicine.utah.edu/dfpm/inhance). In Russian Federation, such a consortium is the National Association of Biobanks and Biobanking Specialists (NASbio) [6]. Hitherto, the association comprises several biobanks, including biobanks solely focusing on aspects and needs of translational oncology (http://nasbio.ru/), but there are also other biobanks that are not members of the NASbio association, and biobanks not related to oncology. There are no RPDCB consortia established in Russian Federation yet.

Methodological approaches and repertoire of biobanked material

Historically, biobanks collected predominantly DNA, blood, frozen tumour tissue samples (diagnostic biopsies, autopsy samples, excess tissue from surgery, etc), and formalin-fixed paraffin-embedded (FFPE) blocks. Recent advances in “omics” studies (transcriptomics, genomics, proteomics, metabolomics, epigenomics, microbiomics, etc), development of 3D tissue culture systems, as well as big-data bioinformatic analysis tools and approaches revolutionized biobanking and led to significant advance in its capabilities, at the same time expanding the methodological approaches to biobanking and repertoire of material to be biobanked.

One of the most accurate in vitro models of solid tumor behavior are three-dimensional (3D) multicellular models, especially the scaffold-based systems including elements of the tumor tissue environment, such as the extracellular matrix (ECM) [10, 11]. There are notable differences between 2D and 3D cell culture models of HNC in terms of sensitivity to drugs and other tumor characteristics [12]. A valuable tool for creating 3D cell systems is decellularized ECM (dECM) prepared from animal tissues, production of which, for a number of reasons, including ethical ones, is a more feasible task than obtaining materials from humans. Currently, such 3D HNC models utilizing dECM derived from animal tissues are being developed [13]. Hence, for example when studying tumour pathogenesis and predicting the response of tumour cells to therapy (personalized therapy), its possible to roughly evaluate the behavior of tumor cells in a 3D model consisting of HNC cells obtained from patient and extracellular decellularized matrix of animals obtained from a biobank (taking into account differences in the ECM from the healthy and malignant tissue micro-environment and also obvious differences between the species). Biobanking of animal tissue for the needs of applied medicine is cost-efficient. Firstly, it allows to use all tissues from the same animal by several research teams, minimizing the total cost of the studies. Secondly, the teams that apply to the biobank for usage of animal tissues do not have to have expertise in working with animals or have an animal facility in their research center. Finally, biobanking of animal tissues will also allow to develop and optimize methods and

approaches to cryopreservation and revitalization of human tissues for the needs of translational oncology. It's important to note that components of patient's tumor micro-environment (TME) itself, including ECM, are promising targets for therapy [14], thus human TME specimens should also be biobanked if feasible.

Currenrtly, in the field of HNC study, rapidly grows the usage of so-called "living biobanks" of the patient-derived 3D tumor cell culture models [15]. Patient-derived xenograft and organoid platforms are instrumental to study the tumour microenvironment in HNC and for co-clinical precision therapy guiding, as outlined in the recent comprehensive review [16]. Organoid cultures provide a suitable model for clonality studies and precision therapeutics [17]. They also can be used for preclinical research of HNC, as demonstrated [18], and recapitulate genomic/transcriptomic characteristic of the patient tissue, for example EGFR expression levels [19].

As for transcriptomics, it is of particular interest to study transcriptome of individual cells (single-cell RNA sequencing, scRNA-seq), since tumors are represented by cells of different types with different patterns of gene expression. Such patterns can not be evaluated when analyzing the bulk RNA transcriptome, and as a result we do not understand the role of particular subpopulations of cells in cancer development, or their role in response to the treatment. Comparative transcriptomics of individual cells in different subpopulations, including the data obtained at different stages during the therapy, as gene expression pattern is not static, could provide valuable data that cannot be otherwise obtained when analyzing the bulk transcriptome. For example, cell-type-specific gene expression signatures of the stromal, cancer, and TME cells in HNC have been characterized recently by scRNAseq using collection of solid tissues and corresponding peripheral blood from HNC patients, which allowed to predict therapeutically targetable checkpoint receptor-ligand interactions [20].

Biobanks to study tumour genetic heterogeneity

Intra-tumour genetic heterogeneity is a well-known clinical challenge, including in HNC [21]. Cells with a different spectrum of oncogenic mutations may be present within the same tumor tissue, partially as a result of a tumor genomic instability. Moreover, during the therapy tumors constantly "evolve" and may acquire new mutations that, subsequently, increases resistance to therapy. Thus, within the framework of approaches known as personalized therapy and pharmacogenetics (selection of medication based on the patient's genotype), it is necessary to assess the genetic heterogeneity of the tumor during the course of treatment, in search for 'targetable genomic alterations' (alterations resulting in a target against which a medication exists), for example RAS or EGFR mutations in HNC (reviewed in [22]). This can become possible with the aid of biobanking of multiple biopsies during the treatment to monitor response to the therapy, and adjust/change it accordingly. Additional screening for nucleotide variants that are not associated with the oncogenesis per se, but may affect pharmacokinetics during the chemotherapy is important to select the optimal treatment dose and regimen. It is also worth assessing the genetic and phenotypic heterogeneity of tumor cells before and after cryopreservation for biobanking, that is, to check how cryopreservation and subsequent revitalization change the cellular composition of the tumor and particular subpopulations within the tumor. It is important to select the optimal method of cryopreservation and revitalization to preserve the native heterogeneity of the sample, which makes it a representative model of the in vivo tumour. When taking and genotyping a biopsy from one part of the tumor, there is a high probability that the full spectre of oncogenic mutations of the neoplasm may not be detected, therefore, along with a tumour tissue biopsy, other clinically informative samples for genotyping should be biobanked, for example, cerebrospinal fluid, whole blood, saliva, urine, etc, allowing for detection of cell-free circulating DNA derived from the tumor cells [23, 24]. Here we emphasize that the genotype profiles of many rare HNC types remain unknown [25] and need to be characterised.

Promising approach in personalized medicine is a comprehensive genetic screening, for example whole genome sequencing not only of the DNA from tumor cells, but from immune cells in the tumor microenvironment, and cells from other tissues of the same patient, which might be targets of metastasis. Such genetic screening allows to identify new genes and nucleotide variants involved in the cancer pathogenesis and response to the therapy.

Pre-emptive medicine and pre-diagnostic material biobanking

Additionally, biobanking can provide a unique opportunity for detection of the cancer-associated viruses in pre-diagnostic samples (such as papillomavirus 16 associated with a subset of head and neck squamous cell carcinomas), and search for avoidable causes of cancer. For example, genotyping of the samples from UK biobank was used to assess the causal effect of cholesterol lowering on risk of HNC [26], another study based on UK Biobank's resources and focused on preventable causes of HNC investigated an association between alcohol consumption and the likelihood of developing HNC [27], and circulating tumor human papillomavirus DNA was detected in biobanked samples before HNC diagnosis [28].

Moreover, biobanking provides an opportunity to discover novel therapeutic targets and develop risk prediction models. For example, analysis of the HNC biopsy samples and corresponding healthy tissue samples provided by two national biobanks integrated into the National Biobanks Network in Spain, allowed to identify novel predictive marker and therapeutic target, glycosphingolipid globotriaosylceramide [28]. Studies based on materials from one of the world's largest biobanks, the UK Biobank, allowed to create a model of the risk for developing HNC [29].

Microbiota biobanking for translational oncology

Undoubtedly, it is expedient to include samples of human microbiome (microbiota) in the nosological biobank collections. Biobanking of the patient's microbiota will further provide an opportunity to build in vitro models of the relationship between the microbiota and the development of malignant neoplasms. There is an association between the microbiome of the oral cavity, pharynx, throat and the HNC [30–32]. Moreover, in oral squamous cell carcinoma an association of oral microbiome with lymph node metastasis was found recently [33]. Taking microbiome samples from the oral cavity is a simple, non-invasive process, which makes it especially attractive for biobanking and creates new avenues for diagnostics and therapy based on the microbiome.

Biobanking for longitudinal studies

In addition, the resources of biobanks can be used to predict the long-term consequences of the disease, side effects from treatment, as well as to compare the course of the disease and treatment depending on various common comorbidities, such as diabetes, cardiovascular diseases, etc. In light of the recent COVID-19 pandemic, it's plausible to propose that biobank resources may be used to optimise the therapy approaches for the HNC patients affected by COVID-19.

The modern classification of neoplasms is often based mainly on the pathomorphology and immunohistochemistry data. Therefore, using biobanks for the accumulation of a large amount of novel data from "omics" studies, longitudinal studies, including samples from different geographical locations and ethnic groups, can help to revisit the classification of tumors, thus increasing diagnostics accuracy and therapy efficiency. Aforementioned, biobanking can allow to find novel diagnostic and prognostic biomarkers based on analysis on biobanked 'omics' data. For example, recent longitudinal study of the patient's plasma proteome demonstrated that these data can be used to detect HNC [34].

Post-mortem biobanking

For many types of HNC, surgical resection of tumors is not possible due to the peculiarities of the localization of the tumor, including in the case of a diffuse nature of localization or aggressive metastasis. In such case, post-mortem biobank collections of the tissue can be an alternative option to collect study material. However, the creation of post-mortem banks is a difficult task for a number of ethical and technical reasons.

Biobanking to study rare cancers

Based on all above mentioned, it is undoubtedly clear that biobanking represents an unparalleled opportunity to study rare, orphan diseases. According to Federal Law No. 323-Ф3 of the Russian Federation "On the Basics of Protecting the Health of Citizens in the Russian Federation", orphan (rare) diseases are diseases that have an incidence of no more than 10 cases per 100000 people. Rare diseases are "individually rare, but collectively common" [35], or "although rare in isolation, are not rare in aggregate", collectively affecting up to 7% of the whole population [36]. However, due to the rare occurrence of such diseases, and therefore luck of the deep knowledge of their etiology, pathogenesis and clinical manifestation, patients with orphan diseases are at risk of misdiagnosis. For this category of patients, the identification of novel diagnostic and prognostic biomarkers, as well as best therapeutic approaches, is urgently needed, whereas insufficient amount of biological material from such patients, and small study cohorts, makes it challenging to perform corresponding clinical and pre-clinical studies. Thus, the use of biobanks allowing to collect a sufficient amount of biomaterial from such patients is almost the only way to address these challenges. Such approach has proven successful in case of several types of rare cancers, such as cholangiocarcinoma [37] or some rare childhood cancers [38]. Patients with rare HNC, for example salivary gland cancer (SGC) [39], might benefit from biobanking too. Indeed, in a recent study, the pooling of the resources from three different biobanks allowed to collect sufficient material to study rare type of HNC [40]. It is important to note that patient with common type of the cancer may also have a rare condition of a different nature, affecting the course of the disease. In this case, the resources of the biobank will make it possible to assess the impact of such rare disease on the course of the oncopathology.

Overall, in light of the current advances in biobanking and associated technologies/methodological approaches, we envision the key role of the biobanks as a platform to study not only common, but also rare types of cancer – the unmet need in contemporary translational oncology.

REFERENCES

1. *Fransson M.N., Rial-Sebbag E., Brochhausen M., et al. Toward a common language for biobanking. Eur J Hum Genet. 2015 Jan;23:22-8.*
2. *Kuzbagarova E., Kuzbagarov A., Shcherbakov A. Legal Framework for Design, Construction, and Operation of Cryobanks in the Russian Federation. In Proceedings of ECSF 2021. Springer, Cham. 2023;151-156.*
3. *Annaratone L., De Palma G., Bonizzi G., et al. Basic principles of biobanking: from biological samples to precision medicine for patients. Virchows Arch. 2021 Aug;479(2):233-246.*
4. *Chróścicka A., Paluch A., Kalaszczyńska I., et al. Biobank personnel—The key to its success. Alternatives to Laboratory Animals. 2022 Jul;50(4):275-81.*
5. *Kinkorová J. Education for future biobankers - The state-of-the-art and outlook. EPMA Journal. 2021 Dec;15-25.*
6. *Anisimov S.V., Meshkov A.N., Glotov A.S., et al. National association of biobanks and biobanking specialists: new community for promoting biobanking ideas and projects in Russia. Biopreservation and Biobanking. 2021 Feb 1;19(1):73-82.*
7. *Doludin Y.V., Borisova A.L., Pokrovskaya M.S., et al. Current best practices and biobanking recomedations. Klin Lab Diagn. 2019 Jan;64(12):769-776.*
8. *Kinkorová J. Biobanks in the era of personalized medicine: objectives, challenges, and innovation. EPMA Journal. 2016 Feb 22;7(1):4.*
9. *Patil S., Majumdar B., Awan K.H., et al. Cancer oriented biobanks: A comprehensive review. Oncol Rev. 2018 May 11;12(1):357.*
10. *Petersen E.V., Chudakova D.A., Skorova E.Y., et al. The extracellular matrix-derived biomarkers for diagnosis, prognosis, and personalized therapy of malignant tumors. Frontiers in oncology. 2020 Dec 18;10:575569.*
11. *Bonartsev A.P., Lei B., Kholina M.S., et al. Models of Head and Neck Squamous Cell Carcinoma Using Bioengineering Approaches. Critical Reviews in Oncology/Hematology. 2022 May 21:103724.*
12. *Melissaridou S., Wiechec E., Magan M., et al. The effect of 2D and 3D cell cultures on treatment response, EMT profile and stem cell features in head and neck cancer. Cancer cell international. 2019 Jan 14;19:16.*
13. *Mascort J.K. Characterization of Decellularized Porcine Tongue: A Matrix for 3D in vitro Head and Neck Cancer Models. McGill University (Canada)). 2019.*
14. *Zaryouh H., Vara-Messler M., Vignau J., et al. Microenvironment-driven intratumoral heterogeneity in head and neck cancers: clinical challenges and opportunities for precision medicine. Drug Resistance Updates. 2022 Jan 25:100806.*
15. *Suryaprakash R.T.C., Kujan O., Shearston K., et al. Three-Dimensional Cell Culture Models to Investigate Oral Carcinogenesis: A Scoping Review. Int. J. Mol. Sci. 2020 Dec 14;21(24):9520.*
16. *Lee T.W., Lai A., Harms J.K., et al. Patient-derived xenograft and organoid models for precision medicine targeting of the tumour microenvironment in head and neck cancer. Cancers. 2020 Dec 12;12(12):3743.*
17. *Li X., Francies H.E., Secrier M., et al. Organoid cultures recapitulate esophageal adenocarcinoma heterogeneity providing a model for clonality studies and precision therapeutics. Nat Commun. 2018;9:2983.*

18. Sun S., Zhang Z. Patient-derived xenograft platform of OSCC: a renewable human bio-bank for preclinical cancer research and a new co-clinical model for treatment optimization. Front. Med. 2016 Mar;10(1):104-10.
19. Driehuis E., Spelier S., Beltrán H.I., et al. Patient-derived head and neck cancer organoids recapitulate EGFR expression levels of respective tissues and are responsive to EGFR-targeted photodynamic therapy. Journal of clinical medicine. 2019 Nov 5;8(11):1880.
20. Kürten C.H., Kulkarni A., Cillo A.R., et al. Investigating immune and non-immune cell interactions in head and neck tumors by single-cell RNA sequencing. Nature communications. 2021 Dec 17;12(1):1-6.
21. Solis R.N., Silverman D.A., Birkeland A.C. Current Trends in Precision Medicine and Next-Generation Sequencing in Head and Neck Cancer. Current treatment options in oncology. 2022 Feb;23(2):254-267.
22. Galot R., Le T.C., Guigay J., et al. Personalized biomarker-based treatment strategy for patients with squamous cell carcinoma of the head and neck: EORTC position and approach. Annals of Oncology. 2018 Dec 1;29(12):2313-27.
23. Patel A., Patel S., Patel P., et al. Saliva Based Liquid Biopsies in Head and Neck Cancer: How Far Are We From the Clinic? Frontiers in Oncology. 2022 Mar 21;12:828434.
24. Spector M.E., Farlow J.L., Haring C.T., et al. The potential for liquid biopsies in head and neck cancer. Discov Med. 2018 May;25(139): 251-257.
25. Morris L.G.T., Chandramohan R., West L., et al. The Molecular Landscape of Recurrent and Metastatic Head and Neck Cancers: Insights From a Precision Oncology Sequencing Platform. JAMA Oncol. 2017 Feb 1;3(2):244-255.
26. Gormley M., Yarmolinsky J., Dudding T., et al. Using genetic variants to evaluate the causal effect of cholesterol lowering on head and neck cancer risk: A Mendelian randomization study. PLOS genetics. 2021 Apr 22;17(4):e1009525.
27. Ingold N., Amin H.A., Drenos F. Alcohol causes an increased risk of head and neck but not breast cancer in individuals from the UK Biobank study: A Mendelian randomisation analysis. medRxiv. 2019 Jan 1:19002832.
28. Rettig E.M., Faden D.L., Sandhu S., et al. Detection of circulating tumor human papillomavirus DNA before diagnosis of HPV-positive head and neck cancer. International Journal of Cancer. 2022 Mar 9.
29. McCarthy C.E., Bonnet L.J., Marcus M.W., et al. Development and validation of a multivariable risk prediction model for head and neck cancer using the UK Biobank. International Journal of Oncology. 2020 Nov 1;57(5):1192-202.
30. Wang L., Ganly I. The oral microbiome and oral cancer. Clinics in laboratory medicine. 2014 Dec 1;34(4):711-9.
31. Gholizadeh P., Eslami H., Yousefi M., et al. Role of oral microbiome on oral cancers, a review. Biomedicine & Pharmacotherapy. 2016 Dec;84:552-558.
32. Frank D.N., Qiu Y., Cao Y. et al. A dysbiotic microbiome promotes head and neck squamous cell carcinoma. Oncogene 41. 2022 Feb; 41(9):1269-80.
33. Eun Y.G., Lee J.W., Kim S.W., et al. Oral microbiome associated with lymph node metastasis in oral squamous cell carcinoma. Scientific reports. 2021 Nov 30;11(1):1-0.
34. Lee J.Y., Shi T., Petyuk V.A., et al. Detection of Head and Neck Cancer Based on Longitudinal Changes in Serum Protein Abundance. Cancer Epidemiology, Biomarkers & Prevention. 2020 Aug;29(8):1665-1672.
35. Conradie E.H., Malherbe H., Hendriksz C.J., et al. An overview of benefits and challenges of rare disease biobanking in Africa, focusing on South Africa. Biopreservation and Biobanking. 2021 Apr 1;19(2):143-50.
36. Chung B.H., Chau J.F., Wong G.K. Rare versus common diseases: a false dichotomy in precision medicine. NPJ Genomic Medicine. 2021 Feb 24;6(1):1-5.
37. Mulvenna J., Yonglitthipagon P., Sripa B., et al. Banking on the future: biobanking for "omics" approaches to biomarker discovery for Opisthorchis-induced cholangiocarcinoma in Thailand. Parasitology international. 2012 Mar 1;61(1):173-7.
38. Hermansen J.U., Wojcik D.M., Robinson N., et al. The Norwegian childhood cancer biobank. Cancer Reports. 2022 Aug;5(8):e1555.
39. van Herpen C.M.L. Patients with Rare Head Neck Cancers: Do They Need a Different Approach?. Critical Issues in Head and Neck Oncology. Springer, Cham. 2021;309-315.
40. Morfouace M., Stevovic A., Vinches M., et al. First results of the EORTC-SPECTA/Arcagen study exploring the genomics of rare cancers in collaboration with the European reference network EURACAN. ESMO Open. 2020 Dec;5(6):e001075.

Поступила 22.09.22
Получены положительные рецензии 05.10.22
Принята в печать 15.10.22
Received 22.09.22
Positive reviews received 05.10.22
Accepted 15.10.22

Contribution of the authors: *Petersen E.V., Chudakova D.A., Shiryaev A.A., Khrushchova A.M., Karalkin P.A., Reshetov I.V. – review of publications on the topic of the article, data collection, analysis of the obtained data, writing the text of the manuscript. Shabalina E.Y., Shaker A.A.S., Chernov T.A. – data collection, analysis of the obtained data, writing the text of the manuscript, editing.*

Вклад авторов: *Петерсен Е.В., Чудакова Д.А., Ширяев А.А., Хрущова А.М., Каралкин П.А., Решетов И.В. - обзор публикаций по теме статьи, сбор данных, анализ полученных данных, написание текста рукописи. Шабалина Е.Ю., Шакер А.А.С., Чернов Т.А. – сбор данных, анализ полученных данных, написание текста рукописи, редактирование.*

Information about the authors:

Petersen Elena Vladimirovna – M.D., Ph.D, Biologist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region, Russia, 141701 E-mail: Petersen.ev@mipt.ru. ORCID: http://orcid.org/0000-0002-8150-7553

Chudakova Daria Aleksandrovna – Ph.D, Biologist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region, Russia, 141701 E-mail: chudakova.da@mipt.ru. ORCID: http://orcid.org/0000-0002-9354-6824

Shiryaev Artyom Anatolievich – M.D., Ph.D.,, Surgeon doctor, I.M. Sechenov First Moscow State Medical University. Address: Moscow, Russia, 8 Trubetskaya St., bld. 2, 119991 E-mail: artemdoc@mail.ru. ORCID: http://orcid.org/0000-0001-9421-420X

Khrushchova Anastassia Mikhailovna – Ph.D., Biologist, A.N. Severtsov Institute of Ecology and Evolution, Russian Academy of Sciences. Address: 33 Leninsky Prospekt, Moscow, 119071 E-mail: cricetulus@yandex.ru. ORCID: https://orcid.org/0000-0002-3956-8395

Shabalina Evgeniya Yurievna – M.Sc, Biologist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region, Russia, 141701 E-mail: evgenyashb@mail.ru. ORCID: http://orcid.org/0000-0002-8184-7363

Shaker Abanoub Ashraf Saleh – B.Sc, Biologist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region, Russia, 141701 E-mail: Shaker.a@phystech.edu. ORCID: http://orcid.org/0000-0002-3025-6504

Chernov Timur Alexandrovich – Ph.D., Biologist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region,

Russia, 141701 E-mail: chtimur@yandex.ru. ORCID: https://orcid.org/0000-0002-7784-7045

Karalkin Pavel Anatolievich – M.D., Ph.D., Biochemist, Moscow Institute of Physics and Technology. Address: 9 Institute Lane, Dolgoprudny, Moscow Region, Russia, 141701 E-mail: pkaralkin@gmail.com. ORCID: http://orcid.org/0000-0002-2838-0776

Reshetov Igor Vladimirovich – M.D., D.Sc., Oncologist, I.M. Sechenov First Moscow State Medical University. Address: 119991, Moscow, Russia, 8 Trubetskaya St., bld. 2 E-mail: reshetoviv@mail.ru. ORCID: http://orcid.org/0000-0002-3888-8004

Информация об авторах:

Петерсен Елена Владимировна – к.м.н., биолог, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, 9. E-mail: Petersen.ev@mipt.ru. ORCID: http://orcid.org/0000-0002-8150-7553

Чудакова Дарья Александровна – к.б.н., биолог, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, 9. E-mail: chudakova.da@mipt.ru. ORCID: http://orcid.org/0000-0002-9354-6824

Ширяев Артем Анатольевич – к.м.н., врач-хирург, Первый Московский государственный медицинский университет имени И.М. Сеченова. Адрес: Москва, Россия, ул. Трубецкая, д. 8, стр. 2, 119991. E-mail: artemdoc@mail.ru. ORCID: http://orcid.org/0000-0001-9421-420X

Хрущова Анастасия Михайловна – к.б.н., биолог, Институт проблем экологии и эволюции имени А.Н. Северцова Российской академии наук. Адрес: 119071, Москва, Ленинский проспект, 33. E-mail: cricetulus@yandex.ru. ORCID: https://orcid.org/0000-0002-3956-8395

Шабалина Евгения Юрьевна – магистр биологических наук, биолог, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, дом 9. E-mail: evgenyashb@mail.ru. ORCID: http://orcid.org/0000-0002-8184-7363

Шакер Абануб Ашраф Салех – бакалавр биологических наук, биолог, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, 9. E-mail: Shaker.a@phystech.edu. ORCID: http://orcid.org/0000-0002-3025-6504

Чернов Тимур Александрович – к.б.н., биолог, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, 9. E-mail: chtimur@yandex.ru. ORCID: https://orcid.org/0000-0002-7784-7045

Каралкин Павел Анатольевич – к.м.н., биохимик, Московский физико-технический институт. Адрес: 141701, Россия, Московская область, Долгопрудный, Институтский переулок, 9. E-mail: pkaralkin@gmail.com. ORCID: http://orcid.org/0000-0002-2838-0776

Решетов Игорь Владимирович – д.м.н., онколог, Первый Московский государственный медицинский университет имени И.М. Сеченова. Адрес: 119991, Москва, Россия, ул. Трубецкая, д. 8, стр. 2. E-mail: reshetoviv@mail.ru. ORCID: http://orcid.org/0000-0002-3888-8004