Original Research

ONCOLOGY

Developing cancer biobanks in Romania: understanding the knowledge and recommendations in assessing a clinical dataset for biospecimens

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Abstract

Background and aims. In the context of the novelty of personalized medicine and biobanking in Romania, there is an acute need to analyze the degree of knowledge of the key actors in the domain. The present study sought to investigate the understanding of 'biobanking' and 'personalized medicine' in three categories of participants in the development of a biobank – health professionals (clinicians/ diagnosticians), scientific researchers, and patients, in order to identify possible faults regarding the level of information. The secondary objective of this study was to identify key elements and relevant data that should be detailed in the clinical dataset that accompanies a biological sample.

Methods. A total of 120 participants were included in this study that were divided into three categories that represent key actors in the development and management of a cancer biobank – clinicians (n=40), scientific researchers (n=40), and oncology patients (n=40).

Results. The survey indicated that the terms 'biobank' and 'personalized medicine' are unknown only in a proportion of patients, while for the other two groups, these terms are already known. The second questionnaire allowed the arrangement of a recommended clinical dataset to be filled when a biological sample is provided to be included in a cancer biobank.

Conclusions. The trust of patients and healthcare professionals in building biobanks that adhere to ethical and operational standards in Romania is important, as the development of artificial intelligence and databases allows advanced knowledge and connection of findings from different databases and, therefore, brings the concept of personalized medicine closer to the clinical practice. The information included in this dataset will be integrated and constitutes a comprehensive biobank database. All these aspects are meant to increase the utility of the specimens in cancer research, as clearly annotated samples, along with prospective data, bring valuable knowledge that helps scientific researchers and clinicians make the clinical connection between the molecular alterations and the phenotype of particular patients or a disease.

Keywords: biobank, personalized medicine, translational medicine, clinical database, biospecimens

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Background and aims

The purpose of a biobank is to systematically collect biological samples alongside the information relevant to each participant [1]. Based on the type and purpose of the biobank, the samples may vary from blood to other biological fluids (saliva, urine), stool, and surgically resected tissue samples (tumor and non-tumor). An important aspect is that these samples need to be backed by additional information regarding the time of sampling, collection method, and storage [2]. Also, an ideal concept of health information that accompanies any sample to be included in the biobank consists of data regarding the medical conditions, treatments, lifestyle, exposure to different chemical/physical/mechanical agents etc., for an accurate assessment of the factors that determine a specific phenotype [3]. In general, the participants that provide their informed consent for the storage of the samples in a biobank must sign the so-called open informed consent meaning that the samples will be used in various future projects whose designs and features cannot be detailed at the moment of the enrollment [4].

The current framework is related to changes in the scientific context, as there is an increased number of samples and data generated using the advanced technologies available nowadays, institutions involved in biobanking, as well as the range of complex diseases indicate that biobanks are an essential resource in the creation and validation of new diagnostic markers and new treatments due to the vast quantity of information stored in the samples, as well as in the clinical information accompanying the biospecimens [5,6]. Biobanks represent an essential resource in the field of cancer research with applications ranging from genomic, proteomic, and metabolomic-based research to translational studies, molecular diagnostic and therapy, identification of therapeutic targets, and the discovery of biomarkers and drugs. Nowadays, biobanks represent a vital element in research, as they represent an important resource for education, favorizing the interconnection of stakeholders in research and they bring a contribution to the validation of standards in clinical pathology [7]. In the context of the novelty of personalized medicine and biobanking in Romania, there is an acute need to analyze the degree of knowledge of the key actors in the domain in order to overcome the obstacles in developing a functional biobank that would respect the recommendations for biobanks in Europe, that include protection of fundamental rights (data protection), use of human tissue in research, mechanisms to involve and engage the public etc. [5]. The present study aimed to investigate the understanding of 'biobanking' and 'personalized medicine' in three categories of participants in the development of a biobank – health professionals (clinicians/diagnosticians), scientific researchers, and patients, in order to identify possible faults regarding the level of information. Another purpose of this study was to identify key elements and relevant data that should be detailed in the clinical dataset that accompanies a biological sample. These data will be integrated and constitute a comprehensive biobank database that will allow the maximization of information extracted from the biological samples. The advantages of this approach are linked to respondent anonymity, which encourages the provision of accurate data and gathering a sufficient number of participants, the possibility of understanding and interpreting the differences among different categories of responders, and less chance of bias when using a standard set of questions/types of answers. The disadvantages are mainly related to the existence of open-answer questions, which interferes with performing a relevant statistical analysis of these answers.

Methods

The present study was approved by the hospital and the institutional ethics committee of Iuliu Hatieganu University of Medicine and Pharmacy no. 80/11.03.2019 and of 'Ion Chiricuta' Oncology Institute in Cluj-Napoca, Romania no. 99.1/04.05.2018. For the purpose of the study, a questionnaire that targets diagnosticians/clinicians, scientific researchers, and patients was applied to investigate the relevant health information to be detailed in the clinical dataset that will accompany the biological sample to be included in a biobank. These data will be used to create a database of the biobank that will contribute to the maximization of the information that can be extracted by analyzing the samples in the biobank. Moreover, another questionnaire regarding the knowledge level of the Romanian population regarding biobanking and personalized medicine concepts was conducted (Figure 1).

Participants and data collection

These two questionnaires were administered to 120 participants that were divided into three categories - 40 clinicians, 40 scientific researchers, and 40 oncology patients. Demographic data were collected from the participants, including age, gender, living background (urban or rural), and education level. The first questionnaire included questions regarding biobanking and personalized medicine concepts and their development in Romania. The first six questions were single-choice, and the last four were open-answer questions, as emphasized in table II. The second questionnaire included information that should be contained in a clinical dataset for a biological sample to be included in a cancer biobank. Participants that completed this questionnaire were asked to rate their agreement regarding the relevant information in a clinical dataset for the biobank in single-choice answers as "yes", "no", and "other".

Figure 1. Study purpose and workflow.

Table I. Demographical characteristics of the study participants.

Characteristics		Scientific researchers (n=40)	Clinicians (n=40)	Oncology patients (n=40)
Gender	F	30 (75)	25 (62.5)	34 (85)
	M	10 (25)	15 (37.5)	6 (15)
Background	Urban	37 (92.5)	39 (97.5)	22 (55)
	Rural	3 (7.5)	1 (2.5)	18 (45)
Age	<20	0 (0)	0 (0)	1 (2.5)
	21-30	9 (22.5)	15 (37.5)	4 (10)
	31-40	15 (37.5)	17 (42.5)	5 (12.5)
	41-50	11 (27.5)	5 (12.5)	9 (22.5)
	51-60	5 (12.5)	3 (7.5)	11 (27.5)
	>60	0 (0)	0 (0)	10 (25)
Education level	No high school	0 (0)	0 (0)	7 (17.5)
	School of Arts and Crafts	0 (0)	0 (0)	3 (7.5)
	High school	0 (0)	0 (0)	12 (30)
	Post secondary school	0 (0)	0 (0)	4 (10)
	College	7 (17.5)	29 (72.5)	11 (27.5)
	Masters	8 (20)	1 (2.5)	3 (7.5)
	Postgraduate school	1 (2.5)	2 (5)	0 (0)
	Doctoral	23 (57.5)	6 (15)	0 (0)
	Post doctoral	1 (2.5)	2 (5)	0 (0)

Statistical analysis

Categorical answers to the questions were described with absolute frequency and percentages. Associations between the responder category and the question's answers were assessed with a chi-squared test or Fisher exact test (in case expected frequencies were below 5 in more than 20% of the participants). Quantitative continuous data were described by median and first and third quartiles. For all statistical tests, we considered the result as significant when two-tailed p-values were below 0.05. All analyses were carried out with R environment for statistical computing and graphics (R Foundation for Statistical Computing, Vienna, Austria), version 4.1.2.

Results

Demographics and characteristics

Table I summarizes the demographic characteristics of the individuals that completed the questionnaires. A total of 120 participants were included in this study, divided into three categories that represent key actors in the development and management of a cancer biobank – clinicians (n=40), scientific researchers (n=40), and oncology patients (n=40). In the three groups, a majority was represented by women - 75% in the scientific researchers' group, 62.5% in the clinicians' group, and 85% in the patients' group). It can be observed that only in the patients group the living background was more balanced between urban (55%) and rural (45%), while in the other two groups, the proportions in urban areas were 92.5% and 97.5%. In terms of age, the majority of patients were >50 years, while clinicians were 20-40 years, and scientific researchers 31-50 years. As expected, patients covered all education levels, with the exception of postgraduate schools and doctoral and post-doctoral studies, while the participants in the other two groups graduated from college and doctoral studies (Table I).

Table II. Answers of participants in each category to each choice question in the questionnaire regarding biobanking and personalized medicine concept and development in Romania.

Survey question	Answers	Scientific researchers (%)	Clinicians (%)	Oncology patients (%)
1. Did you hear the term 'biobank' before this study?	a. Yes	39 (97.5)	37 (92.5)	17 (42.5)
	b. No	1 (2.5)	3 (7.5)	23 (57.5)
2. Did you hear the term 'personalized medicine' before this study?	a. Yes	40 (100)	40 (100)	24 (60)
	b. No	0 (0)	0 (0)	16 (40)
3. If you were to participate in a research study, what type of institution would you choose?	a. Private	5 (12.5)	3 (7.5)	9 (22.5)
	b. Public	13 (32.5)	21 (52.5)	20 (50)
	c. Public and/or private	21 (52.5)	16 (40)	3 (7.5)
	d. I don't know	1 (2.5)	0 (0)	5 (12.5)
	e. Only settled by the insurance company	0 (0)	0 (0)	1 (2.5)
	f. I wouldn't participate	0 (0)	0 (0)	2 (5)
4. Do you consider biobanks in Romania are at a high level of development?	a. Yes	4 (10)	4 (10)	4 (10)
	b. No	33 (82.5)	24 (60)	5 (12.5)
	c. I don't know	1 (2.5)	5 (12.5)	28 (70)
	d. I don't think so	0 (0)	0 (0)	2 (5)
	e. Other	12 (30)	7 (17.5)	1 (2.5)
5. Do you consider that biobanks are useful in developing new therapeutic strategies in oncology?	a. Yes	38 (95)	39 (97.5)	29 (72.5)
	b. No	0 (0)	0 (0)	0 (0)
	c. I don't know	0 (0)	0 (0)	6 (15)
	d. I think so	2 (5)	1 (2.5)	5 (12.5)
	e. Other	0 (0)	0 (0)	0 (0)
6. Would you be willing to accept and pay for the storage of your biological samples in a biobank for future molecular analyses in the context of lack of standard oncology treatment efficiency?	a. Yes	31 (77.5)	35 (87.5)	27 (67.5)
	b. Yes, depending on the costs	2 (5)	3 (7.5)	3 (7.5)
	c. No	5 (12.5)	0 (0)	4 (10)
	d. I don't know	2 (5)	1 (2.5)	5 (12.5)
	e. I don't think so	0 (0)	1 (2.5)	0 (0)
7. What are the major obstacles in biobanking development in Romania?				
8. Do you think that enrolling in personalized medicine studies by providing biological samples should be reimbursed?				
9. Do you think that the information regarding the data generated in a personalized medicine study would influence your decision to enroll in this type of study?				
10. How do you think anonymization of biological samples in a biobank should be performed in order to respect the GDPR regulations and the participant to be comfortable?				

Table III. Clinical dataset recommended to be attached to the biological sample to be included in a cancer biobank.

DEMOGRAPHIC DATA								
Current date	year	…….	month	…….	day	…….		
Sex	male	□	female	□	other	□		
Birth	year	…….	month	…….	day	…….		
Residence	urban	□	rural	□				
Last education level	no highschool	□	High school	□	college	□	PhD	□
GENERAL INFORMATION (LIFESTYLE)								
Is this the first participation in a research study?	no	□	yes	□				
Working in stressful conditions	no	□	low level	□	medium level	□	high level	□
Working conditions	pollution-free	□	low level pollution	□	medium level pollution	□	high level pollution	□
Coffee consumption (number of coffees per day)	0	□	1-2	□	3-4	□	> 4	□
Smoking status (number of cigarettes per day)	0	□	1-5	□	6-10	□	> 10	□
Alcohol consumption (days per week)	0	□	2	□	5	□	7	□
Consumption of meals based on meat (number per week)	0	□	1-6	□	7-10	□	> 10	□
Energy drinks consumption (number of doses per day)	0	□	1-2	□	3-4	□	> 4	□
Physical activities as walking (number per week)	0	□	1-2	□	3-4	□	> 4	□
Relaxing time (number per week)	0	□	1-5	□	6-10	□	> 10	□
Intensive physical activities (number per week)	0	□	1-2	□	3-4	□	> 4	□
BMI	< 18.5	□	18.5÷24.9	□	25.0÷29.9	□	> 30	□
CLINICAL DATA								
Personal physiological history								
Age of first menstruation	year	……..						
Menstruation modifications	no	□	yes	□	details (if applicable)			
Number of births								
Number of abortions								
Blood type								
Rh								
Cardiovascular diseases	no	□	yes	□	details (if applicable)			
Diabetic status	no	□	type 1	□	type 2	□	type 3	□
Other chronic diseases	no	□	yes	□	details (if applicable)			
Family history								
Family history of cancer	no	□	yes	□	details (if applicable)			
Family history of cardiovascular diseases	no	□	yes	□	details (if applicable)			
Family history of diabetes	no	□	yes	□	details (if applicable)			
Family history of other chronic diseases	no	□	yes	□	details (if applicable)			
Medical history								
Clinical investigations before treatment	no	□	yes	□	details (if applicable)			
Primary tumor	no	□	yes	□	details (if applicable)			
Localization of tumor	no	□	yes	□	details (if applicable)			
Type of tumor	no	□	yes	□	details (if applicable)			
Metastasis	no	□	yes	□	details (if applicable)			
Localization of metastasis	no	□	yes	□	details (if applicable)			
Tumor invasion type	no	□	yes	□	details (if applicable)			
Current and past medications								
Neoadjuvant therapy	no	□	yes	□	details (if applicable)			
Adjuvant therapy	no	□	yes	□	details (if applicable)			
Other relevant medical information	details (if applicable)							

Understanding of biobanks

The survey regarding knowledge of biobanking and personalized medicine in Romania and the answers of the participants are detailed in table II. The terms 'biobank' and 'personalized medicine' were unknown only in a proportion of patients ('biobank' – 57.5% and 'personalized medicine' – 40%), while for the other two groups, these terms were already known as the statistical analysis showed a significant difference among the answers given by the participants in the three groups ($p<0.001$ for both question no. 1 and 2). The answers to these questions are closely related to question no. 4, to which the majority of patients indicated a lack of knowledge, while the majority of the participants in the other two groups agreed that biobanks in Romania did not reach a high level of development. This survey indicated that the majority of participants - with the exception of scientific researchers who equally trust public and/or private institutions (52.5%) - would trust public institutions if they were to participate in a research study (clinicians – 52.5% and patients – 50%) and the majority of participants would accept the storage of their biological samples in a biobank to be used for future molecular analyses if the standard oncology treatment would prove inefficient (77.5%, 87.5%, respectively 67.5%) (Table II). The first questionnaire also included open-answer questions, which are represented by questions 7-10 in table II. The opinions of clinicians and researchers to the seventh question included a lack of resources and data provided to patients regarding the benefits, and the absence of regulations, while the majority of patients declared their knowledge in this domain is insufficient to provide a categorical answer. The question no. 8, regarding the reimbursement for providing biological samples in a personalized medicine study, the majority of participants in all three groups consider the enrollment shouldn't be reimbursed. To question no. 9, a majority of participants in all groups considered that the information regarding the data generated in a personalized medicine study would not influence the decision to enroll in this type of study, and those that responded yes, agreed that information regarding the treatment would influence participation in a study. Regarding the last questions, the majority of participants considered that applying an identification code for the anonymization would make them feel comfortable and would observe the GDPR regulations.

Identification of relevant information to be included in a clinical dataset of a biological sample

The second questionnaire comprised 60 queries that were included in five categories: I – demographic, II – general, III – lifestyle, IV – emotional state, and V – clinical data. Associations between the responder category and the questions answers revealed statistical differences among the answers regarding the presence of queries focused on the emotional state for the majority of queries (4 out of 6), with p-values that range from <0.001-0.02. Taking into consideration the answers provided by participants in all three groups and given the relevance of the data in a cancer biobank, the information regarding the emotional state was not included in the clinical dataset that we recommend to accompany a biological sample in a cancer biobank. In table III, we propose a clinical dataset to be filled when a biological sample is provided to be included in a cancer biobank. The information incorporated in this dataset will be integrated and constitute a comprehensive biobank database. This will allow maximization of the data that can be extracted by analyzing the samples using a variety of molecular techniques for personalized medicine. Therefore, the recommended clinical dataset includes demographic data, general information, and clinical data (Table III). The demographic data category includes identifiable information, such as gender, date of birth, and details regarding the area of residence and education level. In the General (lifestyle) category, the participants are required to indicate some of the habits that define their life-style (food, caffeine, alcohol, smoking, physical activity) and their BMI (body mass index). The last category, Clinical data – sub-cateogorized as Personal physiological history, Medical history, Family history, Current and past medication – integrates essential information for cancer treatment, including data regarding the menstrual cycle and pregnancies (for women), family history of different cancers and cancer-related diseases, and other information regarding tumor type, localization, staging etc.

Discussion

Cancer remains among the leading causes of death and diseases, with 18.1 million new cases of cancer registered worldwide in 2020 [8]. One important aspect in establishing the basis for profitable translational cancer research is closely related to the existence and availability of biological samples of good quality and annotations regarding clinical data. Therefore, the success of a cancer biobank relies on the collaboration between patients and health professionals (clinicians and scientific researchers) to cover all the activities and aspects of creating and supporting a biobank. In the attempt to create and maximize the use of specimens in a biobank, it is essential to have consistent procedures and clinical annotation data to improve the utility of biospecimens [9]. It was previously reported that efforts in recruiting potential participants to biobank studies result in high participation rates, especially when the invitation is personal (face-to-face), and not via letter of invitation [10]. Currently, biobanks with the most thorough datasets collections are those meant for clinical and epidemiological purposes

rather than those focusing on lab research on molecular aspects [9]. The complex molecular aspects that characterize cancer cells are described by Hanahan in the review published in 2022 [11], which emphasizes the 12 hallmarks of cancer, including, among others activation of invasion and metastasis, senescence, phenotypic plasticity, genomic instability, and deregulated cellular metabolism. Given the intricate molecular mechanisms that are distinguished in tumor growth and progression, the necessity of a cancer biobank becomes obvious, especially in Romania, where the diagnosis of cancer patients occurs mainly in the late stages [12].

The present study attempted to identify the relevant clinical data and other information to be included in a clinical dataset of a biological sample to be included in a biobank. By applying a questionnaire to a total of 120 participants that belonged to three categories with key roles in the establishment, administration, and operation of a cancer biobank – clinicians, scientific researchers, and oncology patients, and registering their answers after completion of the questionnaire allowed the selection of the information to be incorporated in the clinical dataset. The recommended clinical dataset conceived considering the questionnaire results and the requirements of a biobank includes demographic data, general information, and clinical data. Demographic data category includes identifiable information, such as gender, date of birth, and details regarding the area of residence and education level, while the category of general information is meant to define lifestyle related to food/caffeine/alcohol consumption, smoking habits, and physical activity levels, BMI and also working conditions. Knowledge related to demographical and general information helps clinicians and researchers to establish the context and the environmental factors that may be reflected in the molecular profile of a patient. Clinical data integrate essential information for cancer treatment, including data regarding the menstrual cycle and pregnancies that are relevant in hormone-driven cancers (breast, ovarian, and endometrial cancers in women), family history of different cancers and cancer-related diseases, and other information regarding tumor type, localization, staging, and details regarding treatment type and duration (Table III). All this information contained in the dataset will allow maximization of the data that can be extracted by analyzing the samples using a variety of molecular techniques for personalized medicine. Therefore, this recommended clinical dataset would ensure sufficient knowledge to investigate particularities regarding the molecular profile of patients/tumors to be further used to answer common clinical questions in translational medicine approaches in a rapid and cost-effective manner and to expand the current evidence base for effective clinical oncology care.

Another purpose of this study was to gather information regarding the knowledge of concepts related to modern medicine, such as 'biobank' and 'personalized medicine' in the Romanian population. The survey indicated that these concepts are familiar to researchers and clinicians/diagnosticians, while not all the patients have previously heard about these terms, neither know the situation concerning biobank development in Romania. This observation clearly indicates the need for current approaches in modern medicine information for the general population and highlight the benefits for patients diagnosed with cancer. On the other hand, the majority of participants declared they would accept the storage of their biological samples in a biobank to be used for future molecular analyses, if the standard oncology treatment proved inefficient (Table II). The trust of patients and healthcare professionals in developing biobanks that are built adhering to ethical and operational standards in Romania is important, as the development of artificial intelligence and databases allows advanced knowledge and connection of findings in different databases and, therefore brings the concept of personalized medicine closer to the clinical practice, with applications in early diagnosis and pharmacogenomics, to predict response to targeted therapy [13-15].

It is worth mentioning that even though the present manuscript focuses on developing a clinical dataset for the biospecimens in a biobank, there is also the need to implement standard operating procedures for handling and storage of these samples in order to improve the standards of biobanking in Romania and to ensure adequate quality for these samples. It is also important that the data in the biobank are always updated with follow-up data for the patients, such as status and survival, as this information is required in most translational cancer research projects [9]. All these aspects are meant to increase the utility of the specimens in cancer research, as clearly annotated samples [16]. Moreover, prospective data bring valuable information that helps scientific researchers and physicians make the clinical connection between the molecular alterations and the phenotype of particular patients or a disease.

The limitations of the current study are related to the open-answer queries in the survey regarding 'biobanks' and 'personalized medicine' concepts understanding. These types of answers hinder one's ability to perform a statistical analysis and assess a systematic categorization of these answers to extract the most relevant information. On the other hand, the existence of open-answers questions opens the possibility to new investigations or information campaigns that are focused on specifically addressing the interests, concerns, and needs of respondents [17].

Conclusions

The present study contributed to the understanding of the perception of the Romanian population of terms and concepts related to modern medicine, indicating that patients are the least informed category in this concern. This observation clearly shows that there is a need to inform the general population about the current approaches in modern medicine, highlighting the benefits for patients diagnosed with complex diseases, especially cancer. In addition, in this study, we managed to systematize a recommended clinical dataset for samples to be included in a cancer biobank. The data included in the dataset are meant to increase the utility of the specimens in cancer research, with comprehensive annotations and prospective data to help health professionals make the clinical connection between the molecular alterations and the phenotype of particular patients or disease and to identify a personalized treatment that would ensure a response to therapy. All these experiments were conducted in order to establish the basis for developing a functional biobank in accordance with the recommendations for Europe regarding data protection and means to involve and engage the patients.

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