

REVIEW ARTICLE



RePo-SUDOE: A Transnational Network for Drug Repurposing in the SUDOE Space

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ABSTRACT

The development of new drugs is hindered by high failure rates, substantial costs, and prolonged timelines, highlighting the importance of drug repurposing (or drug repositioning) as a key strategy to identify new therapeutic applications for existing drugs. Despite its potential, collaboration within the SUDOE space, concerning Portugal, Spain, and France, remains limited, as evidenced by a bibliometric analysis that reveals their relatively modest contribution to global drug repurposing research in comparison to leading countries, such as China, USA, and UK. The RePo-SUDOE project aims to address this gap by bringing together diverse partners to advance drug repurposing technologies and enhance the region's competitiveness in this field. The project includes three key objectives: (i) raising awareness and understanding of drug repurposing technologies, positioning SUDOE's R&D centers as leaders in European research; (ii) fostering multidisciplinary collaboration and identifying opportunities for innovative drug repurposing initiatives across the SUDOE space through the establishment of a

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transnational network with a key focus of developing methodologies for drug repurposing for cancer treatment; (iii) creating a prototype of a three-dimensional visualization room for biological systems with virtual and augmented reality technologies to explore drug—target interactions, engaging STEAM students and researchers in immersive learning. The RePo-SUDOE project brings together diverse partners from the SUDOE space to collaborate on drug repurposing, making scientific information more accessible, and using advanced visualization technologies to strengthen the field in this geographic region.

KEYWORDS

drug repurposing; therapeutic targets; cancer; SUDOE space; transnational network.

DRUG REPURPOSING

The drug discovery process is a lengthy and expensive task, typically requiring 12–15 years for a drug to be approved and brought to market. Also, the efficiency of research and development (R&D) in drug discovery has decreased, taking into account the amount of money invested. Drug repurposing consists of finding new therapeutic indications for existing drugs, different from their original medical application. Therefore, the discovery and knowledge about new molecular targets and pharmacological mechanisms represent novel therapeutic opportunities for clinically used drugs.

In traditional drug discovery, the first step is the identification of a new molecular entity that moves forward to a subsequent hitto-lead optimization, eventually obtaining an optimized drug candidate for further pharmaceutical development.3 The hit-to-lead optimization aims to enhance drug potency, selectivity, and druglike properties. The detailed study of the pharmacological mechanism of the drugs can result in the development of new therapeutic classes. The next steps are the preclinical and clinical trials that will validate the use of the new drug. In drug repurposing, it may be possible to bypass preclinical and Phase I trials, as the safety profile of the existing drug is already established. These drugs can re-enter the development process directly at Phase II clinical trials, where their new therapeutic potential is evaluated for efficacy in treating a different condition.⁴ The drug repurposing approach allows faster drug development with a significant reduction in investment and risk involved.4,5

The main advantage of drug repurposing is the existing knowledge of the drug's safety profile, clinical use, and manufacturing processes. However, several challenges remain. Intellectual property and patent restrictions can hinder repurposing efforts. Clinical validation is essential, as the drug's efficacy for the new indication must still be rigorously demonstrated. Additionally, there is the risk of unforeseen interactions or adverse effects when used in different patient populations. Drug repurposing can have an impact on different diseases, including rare diseases and cancer. Examples of repurposed drugs include aspirin, thalidomide, sildenafil, and dimethyl fumarate.

BIBLIOMETRIC ANALYSIS OF GLOBAL DRUG REPURPOSING

International networks on drug repurposing can be identified through bibliometric analysis. This type of study reveals the lack

of consistent collaboration within the SUDOE space, comprising Portugal, Spain, and France.

For the following bibliometric analysis, data were acquired from the Scopus database. The search was conducted using the combination of the following keywords and terms: (Title (drug repurposing OR drug repositioning) AND (cancer)). Only original articles published in English up to the year 2024 were included.

After data extraction, bibliometric analysis was conducted using VOSviewer software (version 1.6.18). Visual network graphs were generated to illustrate patterns of collaboration between countries and the co-occurrence of keywords. Each term (country or keyword) was represented by a circle, with the size of the circle proportional to its frequency of occurrence (minimum threshold: 5). The proximity between circles reflected the strength of their association, while different colors indicated distinct thematic clusters. The thickness of the connecting lines denoted the strength of the relationships between terms. The main results from this bibliometric analysis are presented below.

Study Selection and Characteristics

A total of 878 publications, published from 2005 to 2024, were identified through our search strategy in the Scopus database. Of these, 374 were excluded because they were not original articles. The titles of the remaining 505 publications were evaluated according to our inclusion criteria. The annual number of publications on cancer-related drug repurposing is presented in **Figure 1**. Prior to 2014, only a few studies were published in this field. A single article was published in 2009 (n = 1), and it was in 2018 that the number of publications began to increase gradually. The highest annual peak of publications was reached in 2023, accounting for 19% (n = 95) of all included publications. Although the number of publications decreased slightly in 2024 (n = 85), a sustained increase in cumulative publications has been evident since 2021, representing 63% of the total output.

Country, Author, and Keyword Analysis

The international cooperation between different countries is shown in Figure 2A, and with a focus on European countries in Figure 2B. A total of 68 countries are represented. The size of each circle is proportional to the extent of each country's contribution; the lines between the circles represent collaborations between countries or regions, and the thickness of the connecting lines indicates the frequency of these collaborations. The highest number

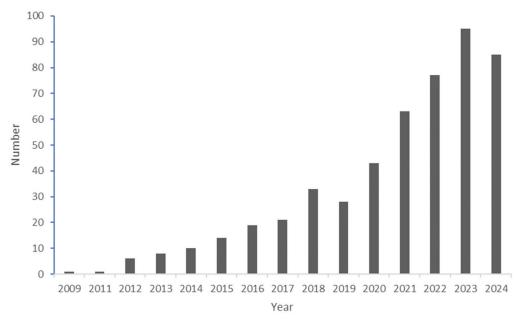


Figure 1. Annual number of original articles on drug repurposing (cancer-related) published between 2009 and 2024, identified through Scopus according to the predefined search strategy and inclusion criteria.

of publications came from China (n=136), followed by the USA (n=108) and India (n=74). Among the European countries, the UK (n=33) and Germany (n=25) are leading contributors. Regarding the SUDOE space, Spain, France, and Portugal are represented with 6, 4, and 5 publications, respectively. The results indicate that France collaborates mostly with Canada, Portugal with Brazil, and Spain with Germany, Turkey, and Mexico.

The visualization map of keywords appearing more than eight times in the cancer-related drug repurposing field is shown in Figure 2C. While some of the keywords were disease-related, including "breast cancer," "glioblastoma," "colorectal cancer," "melanoma," others were associated with specific drugs, such as "metformin" and "mebendazole." Additionally, some keywords were associated with research methodologies, namely, "Molecular docking," "Connectivity map," and "Molecular dynamics simulation."

This short bibliometric analysis underscores the limited and fragmented collaboration among countries within the SUDOE space in the field of cancer-related drug repurposing. Given the growing global interest and the strategic importance of this research area, there is a clear need to promote stronger, more structured, and sustained scientific cooperation among these countries. Enhancing collaboration within this regional framework could lead to greater research visibility, optimized use of resources, and the development of innovative therapeutic strategies with broader impact.

THE REPO-SUDOE PROJECT

The RePo-SUDOE Transnational Network

The main objective of the RePo-SUDOE project is to develop and disseminate advanced technologies for drug repurposing within

the SUDOE space by establishing a transnational network dedicated to this field of pharmaceutical development. This overarching goal aligns with the specific objectives of the SUDOE Programme along three distinct yet complementary dimensions. Strategically, the project aims to foster cooperation and promote territorial cohesion and balance within the SUDOE space. Scientifically, the project will implement, consolidate, and disseminate a range of research and innovation tools aimed at supporting drug repurposing efforts. Finally, from an educational standpoint, the project will contribute to the training and capacity building of highly qualified human resources, who will play a pivotal role in sustaining future activities within this transnational cooperation network.

A key component of the project is establishing formal collaboration among partner institutions to foster synergies and consolidate strategic alliances, ensuring the initiative's long-term sustainability and impact. Within this framework, participating institutions will develop a dedicated cooperation platform to support the joint development of research and innovation projects. This platform will facilitate the involvement of additional partners—particularly from the SUDOE space—and create favorable conditions for broader participation in European research initiatives, thereby contributing to the advancement of scientific knowledge in the field of drug repurposing. This initiative seeks to identify and engage entities interested in participating in drug repurposing projects, culminating in a publicly available list of potential partners hosted on the RePo-SUDOE website.

To facilitate seamless collaboration and knowledge exchange, the project is developing a Virtual Research Environment (VRE)¹⁰ and a mobile Application,¹¹ enabling stakeholders to share ideas, discuss challenges, and disseminate knowledge readily. Annual meetings, including participation in summer schools, technical-scientific workshops, and seminars, will further enhance

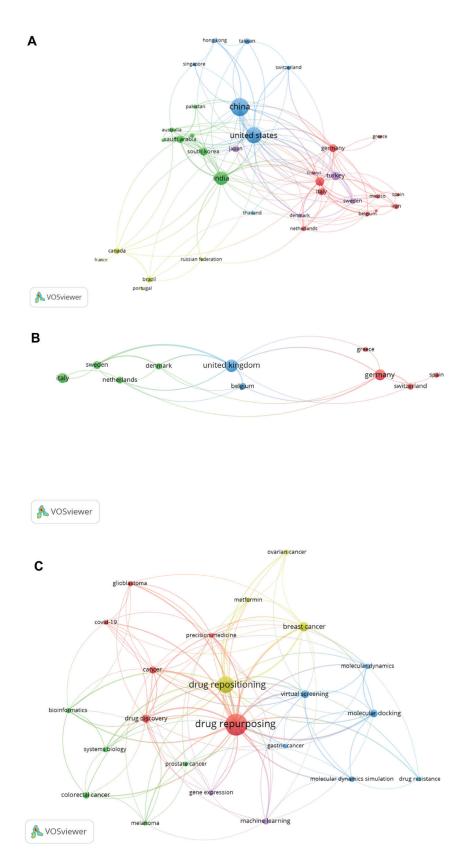


Figure 2. Network visualization maps generated through bibliometric analysis. (A) Global cooperation network of countries; (B) Cooperation network of European countries. (C) Keyword co-occurrence network (threshold ≥8 occurrences). Nodes represent countries or keywords, with node size proportional to the number of publications or keyword occurrences. The thickness of the connecting lines indicates the strength of collaboration or co-occurrence between nodes. Analysis performed using VOSviewer software.

capacity building and knowledge sharing, fostering direct interaction between researchers, industry partners, and other relevant stakeholders.

The project also aims to define priority therapeutic targets and drugs, strategically focusing the network's efforts on areas of highest impact and scientific relevance, such as the treatment of cancer. These integrated initiatives aim to establish a robust and sustainable foundation for cross-border cooperation within the SUDOE space, ultimately strengthening its position as a leading innovation center in drug repurposing.

Scientifically, this cooperation platform will serve as the structural foundation for the implementation of a transnational network on drug repurposing, organized around several key activities that operationalize the project's strategic objectives. A relevant activity will be the development of an open-access, user-friendly database containing comprehensive information on therapeutic targets identified in the scientific literature. Designed as a dynamic and evolving resource, this database currently under development will also integrate contributions from the broader scientific community and other relevant stakeholders—including research centers, healthcare providers, and pharmaceutical industry representatives—thereby ensuring the continuous expansion and updating of knowledge on therapeutic opportunities.

Furthermore, for each identified therapeutic target, drugs or innovative therapies with potential biological activity of relevance to the drug repurposing community will be systematically identified. To complement this effort, computational procedures and methods for evaluating the interaction between drug candidates and therapeutic targets will be developed and made publicly available, primarily through the VRE. These computational tools will also be open to contributions from other researchers, fostering broader collaboration and knowledge sharing. In addition to computational methodologies, the project will develop and disseminate experimental procedures to analyze drug—target interactions, ensuring an integrated and robust assessment pipeline that bridges *in silico* and *in vitro* approaches.¹²

In a longer perspective, another key component will be the systematic compilation of additional data-including in vitro, in vivo, and medical imaging studies—documenting the therapeutic evolution of cases where proposed therapies have been applied to specific targets. This body of evidence will be essential for advancing personalized cancer therapies. To promote knowledge dissemination and further research, images and videos of computational simulations depicting drug-target interactions as well as detailed experimental protocols will be generated and made available to the scientific community. Based on the insights gathered from these activities, the project aims to propose a portfolio of repurposed drugs, as well as novel molecules identified through the drug repurposing studies, specifically for cancer treatment. These candidate molecules should subsequently undergo preclinical testing, and the resulting data should be made available to pharmaceutical companies, thereby contributing to innovation and supporting the development of new therapeutic options.

Finally, the RePo-SUDOE initiative pursues another goal concerning the creation of a prototype for a three-dimensional (3D) $^{\circ}$

visualization room for biological systems. This prototype, for which the first tests were already done, will serve as a model for the development of similar solutions across the SUDOE space. It will be a fundamental tool for training students and researchers in the 3D visualization of biological structures, ¹³ fostering the development of intellectual and visual creativity associated with disease mechanisms and the drug development process. ^{14–18} The achievement of this goal requires a set of integrated activities with a strong educational component.

These activities include the setup of the prototype of the 3D visualization room, where examples of drug—target interactions represented from the RePo-SUDOE database will be displayed. This prototype will be implemented in at least one of the project partners' institutions and will serve as a pilot for the development of similar 3D visualization rooms across the SUDOE territories. The 3D visualization room prototypes are expected to stimulate the institutions and territories where they are implemented through the organization of study visits and the continuous development of the applied technologies. The study visits for young students will allow them to interact with the visualization content by manipulating molecules and biological systems (rotating, zooming, changing representation modes, etc.), thus fostering their interest in the drug repurposing process and in STEAM fields.

To assess the impact of these experiences, evaluation and satisfaction questionnaires will be administered to both students and teachers. Furthermore, health literacy materials will be produced, focusing on drug development and repurposing. Altogether, these activities aim to raise awareness in the educational and research communities about drug repurposing, especially about the technologies involved in drug development.

RePo-SUDOE emphasizes a territorialized and cross-border approach within the SUDOE space, which comprises Portugal, Spain, and France. The initiative brings together a diverse consortium of partners, including higher education institutions, research centers, companies, and civil society organizations. By combining computational and experimental strategies, the project aims to increase the number of successful cases in drug repurposing. Uniquely, it integrates immersive educational technologies and public engagement initiatives to reduce regional disparities and enhance scientific literacy in the emerging field of drug repurposing.

Scientific Pertinence of the RePo-SUDOE Transnational Network

The SUDOE space constitutes a peripheral territory within the EU that faces significant social and economic disparities in access to services and the distribution of resources between rural and urban areas, further intensified by aging and declining populations. In response to these structural imbalances, the RePo-SUDOE project emerges as a strategic and scientifically grounded initiative to promote R&D in the area of drug repurposing.

It is important to highlight the transnational dimension of this project—reflected in the collaboration among diverse partners—that enables a sustainable knowledge and technology transfer from more developed and densely populated regions to less advanced areas. By establishing a cross-border network, this initiative

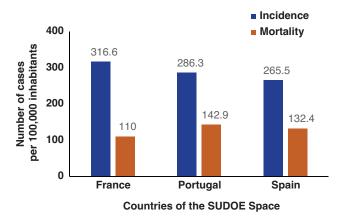


Figure 3. Annual cancer incidence and mortality in the countries of the SUDOE space (France, Portugal, and Spain) in 2022. Incidence and mortality are expressed as the number of cases per 100,000 inhabitants. Data derived from national epidemiological sources. ^{14–16}

enhances coordinated responses to shared challenges, such as adapting to societal transformations, mitigating the effects of population aging, and intensifying efforts to combat diseases such as cancer. A key scientific dimension of RePo-SUDOE is its focus on drug repurposing as an innovative strategy to tackle complex health challenges, particularly cancer, which remains a leading cause of death in all three participating countries. Epidemiological data^{19–21} shown in **Figure 3** highlight the urgency: age-standardized annual cancer incidence rates reach approximately 270 cases per 100,000 inhabitants in Portugal,²⁰ 275 in Spain,²⁰ and 275 in France,²⁰ with corresponding age-standardized mortality rates of 142.9 in Portugal, 132.4 in Spain, and 110.0 in France, as recorded in 2022.

By establishing a cross-border network of researchers, institutions, and stakeholders, RePo-SUDOE seeks to address a critical gap in the SUDOE research landscape—namely, the absence of a transnational structure dedicated to drug repurposing, as illustrated in Figure 2. To address this need, the project embraces an integrated and innovative approach, aiming to make scientific knowledge and advanced visualization technologies widely accessible for the benefit of society. Beyond its scientific objectives, RePo-SUDOE plays a fundamental role in strengthening regional research capacity through the advanced training of highly qualified professionals. These capacity-building efforts will directly contribute to the scientific and technological development of the SUDOE space while also ensuring the long-term sustainability of the network.

Transnational Pertinence of the RePo-SUDOE Network

The RePo-SUDOE project addresses a critical gap in the scientific and technological development of the SUDOE space by establishing a transnational framework for drug repurposing. Recognizing the need for a coordinated, cross-border approach, the project mobilizes a multidisciplinary consortium, ensuring a comprehensive and integrated strategy. Notably, it promotes collaboration between institutions located in more populated regions, such as Bordeaux, A Coruña, and Santiago de Compostela, and less

populated regions, such as Guarda, where the project coordination is based. In this context, transnational cooperation is essential for achieving the project's objectives and expected outcomes, involving a consortium of partners encompassing the entire drug repurposing value chain. This approach aligns with the priorities outlined in the participating regions' Smart Specialization Strategies, which include advancing personalized medicine, improving healthcare delivery, and developing biotechnological and digital solutions. By leveraging these shared strategic priorities, the RePo-SUDOE project significantly strengthens and expands transregional scientific and technological capacities within the SUDOE space.

Concurrently, the project's transnational impact is expected to foster sustainable job creation and reinforce knowledge and technology transfer mechanisms, particularly within the consortium's regions. Therefore, the transnational cooperation that underpins RePo-SUDOE ensures the establishment of a cross-border network for drug repurposing, with a particular emphasis on oncology. This network serves as a strategic cornerstone to catalyze innovation and development across the SUDOE space with the following objectives: (i) fostering greater territorial cohesion among the regions within the SUDOE space, (ii) reducing structural and demographic disparities, and (iii) enhancing the technical and scientific capabilities of the involved territories. It is clear nowadays that initiatives limited to national, regional, or local levels would be insufficient for addressing the challenges faced by consortium partners within their current contexts. In this regard, transnational collaboration provides a vital framework to mobilize complementary technical, scientific, and operational expertise across all partners.

The RePo-SUDOE project also aims to extend beyond the SUDOE space and create synergies with other European and international initiatives in the scope of drug repurposing. Examples of potential collaborative initiatives include REPO4EU,²² REMEDi4ALL,²³ EOSC4Cancer,²⁴ canSERV,²⁵ EUCAIM,²⁶ HEALTHYCLOUD,²⁷ EOSC-Life,²⁸ B1MG,²⁹ EBRAINS,³⁰ and NEWROAD.³¹ Collaboration between different project initiatives boosts European efforts on advancing drug repurposing for extended geographical and societal perspectives.

THE SOCIETAL IMPACT OF THE REPO-SUDOE PROJECT

Main Target Groups

The RePo-SUDOE aims to generate tangible benefits for diverse target groups across the SUDOE space. Key beneficiaries include non-governmental organizations (NGOs) and other interest organizations, which will be able to expand their collaboration networks with higher education institutions and research centers, thereby strengthening their activities in the health sector. In addition to NGOs, the project also brings advantages for universities, companies, hospitals, educational centers, and the general public, promoting scientific advances, new technologies, and greater access to health information. **Table 1** summarizes the primary benefits for the main target groups involved.

Table 1. Summary of the Main Benefits Provided by the RePo-SUDOE Project to Different Stakeholder Groups Across the SUDOE Space

Stakeholders	Main Benefits
Higher education and research organizations	Strengthening of cross-border cooperation.
	• Easy accessible support for the development of both fundamental and applied research projects.
Interest groups, including NGOs	Opportunity to diversify their activities.
	 Increased connections with research and higher education institutions.
Small and medium companies	 Access to technologies for testing drug repositioning.
	 Possibility to repurpose their own proprietary drugs.
Business support organizations	 Opportunity to associate with a transnational cooperation project.
	Support for the development of fundamental and applied research.
Public	 Health literacy actions focused on drug repositioning.
	 Improved access to information and awareness on health issues, especially cancer.
Hospitals and medical centers	 Access to affordable alternatives by repurposing existing drugs and therapies.
	Reduced costs compared to developing new drugs.
Education/training centers and schools	 Opportunity for students to visit the prototype of the 3D visualization room of biological systems.
	 Closer connections to higher education institutions and scientific research projects.
	 Ability to replicate the 3D visualization room prototype in their own facilities.

Broadening Societal Relevance Through Public Health and Equity

Apart from its contributions to literacy, education, and research, RePo-SUDOE is well-positioned to produce wider business advantages in the public health sector. Drug repurposing can have significant social implications for health equity and public health policy. By implementing policies and incentives that ensure equitable access, encourage innovation, and focus on health outcomes, it is possible to reduce disparities in access to repurposed therapies and promote broader health equity objectives.³² The research has the potential to increase access to therapies by finding affordable therapeutic options through drug repurposing, particularly in the SUDOE space with scarce or restricted resources. Repurposed drugs can provide suitable and quicker access to solutions to meet healthcare demands because they frequently have established safety profiles and are less expensive.

Additionally, RePo-SUDOE aims to establish active cooperation with hospital networks, professional associations, national health authorities, and patient advocacy groups to facilitate the dissemination and future adoption of scientific findings. By targeting diseases with significant social and economic impact and implementing dissemination strategies centered on equity, the project not only advances scientific knowledge but also contributes to reducing health disparities across the SUDOE space. RePo-SUDOE intends to collaborate with public health organizations to co-develop targeted and adapted communication strategies, not only for the scientific community but also for the general public, ensuring equitable access to scientific knowledge.

The project will incorporate public health evaluation tools, including satisfaction surveys, to assess the extent to which its dissemination is appropriate and reaches the intended audiences.

Contribution to the Territorial Rebalancing of the SUDOE Space

The SUDOE space is marked by pronounced territorial disparities, particularly evident in the challenges of rural depopulation and accelerated demographic aging. In response to these dynamics,

the present project proposes a multifaceted strategy to contribute to the urban–rural territorial rebalance by fostering interinstitutional, intersectoral, and interregional cooperation throughout the SUDOE area. Central to this initiative is the integration of transnational collaboration in drug repurposing, institutional capacity building, and educational innovation—three interconnected pillars that together form a cohesive and sustainable development framework. This holistic approach addresses scientific and technological challenges while strengthening the foundations for long-term socioeconomic and territorial resilience.

The establishment of a strong transnational network and strategic alliance among project partners is grounded in inclusive collaboration, engaging a wide range of stakeholders across the entire drug development and repurposing value chain. This international structure is designed to stimulate innovation, broaden scientific outputs' impact, and enhance the international visibility of participating institutions. The project aims to contribute to the broader goals of economic improvement in participating regions by reinforcing local research capacity and stimulating innovation-driven growth.

A core component of the project is its emphasis on institutional reinforcement through educational innovation. Among the key initiatives is the development of 3D visualization room prototypes, designed to directly tackle a prevalent learning challenge: the difficulty that many students encounter in mentally conceptualizing 3D molecular structures and, notably, their interactions with different compounds. This limitation constrains academic performance and affects the ability to innovate in professional settings. By incorporating these tools into educational environments—especially within less developed areas of the SUDOE space—the project promotes a more dynamic and inclusive pedagogical model, designed to foster creativity, engagement, and the acquisition of critical skills in STEAM-related fields.

These educational innovations aim to be catalysts for a systemic change. The project aims to foster regional cohesion and reduce demographic imbalances through complementary outreach activities, such as school visits and the replication of prototypes in additional regions. By enhancing the capacity of institutions to train

highly skilled professionals in science and technology, the initiative actively supports sustainable development objectives, strengthening the link between education, innovation, and public health in a transnational context.

Public Engagement and Science Communication

In parallel to its scientific, educational, and literacy dimensions, the RePo-SUDOE project will develop a robust public engagement strategy to promote awareness of drug repurposing and its potential social value. Prototypes of 3D visualization rooms will be made available not only to students but also to the public, including senior citizens and patient groups, transforming them into local science outreach centers.

In addition, public lectures, media campaigns, and interactive web-based tools will be employed to promote scientific culture and stimulate interest in biomedical innovation. Communication materials will be developed in multiple SUDOE area languages (Portuguese, Spanish, and French) to ensure inclusion and regional reach. These activities aim to position drug repurposing as a visible and understandable concept for citizens, increasing transparency and support for biomedical research in society.

CONCLUDING REMARKS

The RePo-SUDOE project presents a comprehensive initiative that responds to critical scientific, societal, and territorial challenges within the SUDOE space. By fostering a transnational network dedicated to drug repurposing, the project not only enhances regional research and innovation capacities but also promotes equitable access to therapeutic advances. Through its focus on diseases with high social and economic burden—particularly cancer—RePo-SUDOE reinforces the role of research in addressing public health priorities.

Furthermore, by integrating advanced visualization technologies, strengthening education and training, and promoting public engagement, the project bridges the gap between science and society. It empowers stakeholders across sectors—research institutions, healthcare providers, NGOs, businesses, and citizens—while actively contributing to territorial cohesion and socioeconomic development in underserved regions.

Ultimately, RePo-SUDOE goes beyond scientific advancement. It builds a resilient and inclusive foundation for long-term cooperation, knowledge exchange, and innovation in drug development, positioning the SUDOE space as a relevant actor in the European health research landscape and as a model for responsible and equitable innovation.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

DATA AND CODE AVAILABILITY

Data and code availability does not apply.

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