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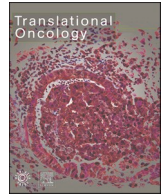
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A regionally based precision medicine implementation initiative in North Africa: The PerMediNA consortium

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ABSTRACT

Precision Medicine is being increasingly used in the developed world to improve health care. While several Precision Medicine (PM) initiatives have been launched worldwide, their implementations have proven to be more challenging particularly in low- and middle-income countries. To address this issue, the “Personalized Medicine in North Africa” initiative (PerMediNA) was launched in three North African countries namely Tunisia, Algeria and Morocco. PerMediNA is coordinated by Institut Pasteur de Tunis together with the French Ministry for Europe and Foreign Affairs, with the support of Institut Pasteur in France. The project is carried out along with Institut Pasteur d'Algérie and Institut Pasteur du Maroc in collaboration with national and international leading institutions in the field of PM including Institut Gustave Roussy in Paris. PerMediNA aims to assess the readiness level of PM implementation in North Africa, to strengthen PM infrastructure, to provide workforce training, to generate genomic data on North African populations, to implement cost effective, affordable and sustainable genetic testing for cancer patients and to inform policy makers on how to translate research knowledge into health products and services. Gender equity and involvement of young scientists in this implementation process are other key goals of the PerMediNA project.

In this paper, we are describing PerMediNA as the first PM implementation initiative in North Africa. Such initiatives contribute significantly in shortening existing health disparities and inequities between developed and developing countries and accelerate access to innovative treatments for global health.

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Introduction

The past several decades has seen enormous progress in the field of genomic medicine [1]. Various efforts, including the Human Genome Project, deep catalogs of human genetic variations, along with the Genome Wide Association Studies (GWAS) revolution and massive sequencing have all resulted in a wealth of knowledge on the genetics of common diseases [2–5]. This includes the discovery of more than 70,000 robust genetic associations to common diseases and traits, and important insights into the underlying basis of some rare diseases [6,7].

In Africa, thanks to initiatives such as the Human Heredity & Health in Africa (H3Africa) consortium [8], the biomedical research field has seen significant advances in genomic data generation and analysis. As part of the H3Africa consortium, the H3ABioNet project (Pan African Bioinformatics network for H3Africa) further acted as a support mechanism to all H3Africa projects [9] and played a key role in building African capacities in bioinformatics and OMICs sciences (genomics, transcriptomics, proteomics, or metabolomics) and contributed to improve and consolidate bioinformatics infrastructure in several African institutions across the continent [9]. However, despite the tremendous efforts of the H3Africa consortium projects, North African cohorts were underrepresented, leading to a gap in data release and analysis in North Africa (NA) [10–12].

In parallel, several projects and initiatives have been conducted by the “Pasteur Network” [13] in the North African region involving Institut Pasteur de Tunis, Institut Pasteur d’Algérie et Institut Pasteur du Maroc in collaboration with Institut Pasteur Paris and other french institutions mainly Institut Gustave Roussy and Institut Marie Curie, which led to important progress in medical and scientific research in the North African region. Yet, there is much more that needs to be done [14, 15].

Compared to Sub-Saharan Africa, NA is experiencing a silent epidemic of non-communicable diseases, including diabetes, metabolic diseases, and cancer. In terms of Precision Medicine application in healthcare and targeted therapies development, medical oncology is undoubtedly one of the most advanced fields [16,17]. Indeed, cancer stands out as one of the most widespread and extensively researched diseases in NA [18–22]. According to the incidence rates from the GLOBOCAN database, breast and lung are the most common cancers in the region [23]. Although all the national and regional efforts and action plans dedicated to fighting cancer, breast cancer (BC) incidence and mortality rates are still increasing dramatically in NA [24]. Moreover, lung cancer (LC) is on the rise in the region in both men and women mainly due to the high number of smokers but also the involvement of the genetic and molecular risk factors [25,26]. A number of studies were conducted in NA on clinically relevant and actionable biomarkers associated with BC and LC, namely *EGFR*, *ALK*, *ROS* and *BRCA* [20,21, 27–30]. The investigation of these actionable genes is very important for PM implementation. However, much more than genomic testing will likely be required to implement PM [31].

Within this context, the PerMediNA project was launched and is considered as the first PM implementation initiative in NA aiming to translate research findings into healthcare practice. Its mission is to develop and roll out a coordinated research infrastructure that is tightly coupled to a well-structured training program. This paper describes the PerMediNA initiatives mission and goals as well as its achievements and future directions.

- PerMediNA initiative

Responding to the challenge of implementing PM in NA, the PerMediNA project was launched to incorporate three North African countries namely Tunisia, Algeria and Morocco into a major international initiative in order to contribute to a successful implementation of PM in the region. PerMediNA is funded by the French Ministry for Europe and Foreign Affairs (MEAE) under the FSPI program (Fond de

Solidarité pour les Projets de l’Innovation) and is coordinated by Institut Pasteur Tunis together with the MEAE, with the support of the Operations Unit of Institut Pasteur Paris and is carried out along with Institut Pasteur d’Algérie and Institut Pasteur du Maroc. Other national and international cancer reference centers and leading institutions in the field of genomics are involved in this project including Gustave Roussy (IGR), Institut de Cancérologie de l’Ouest (ICO) and the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences (Fig. 1).

The project objectives are focused on the assessment of the readiness level for PM implementation in NA, capacity building, training, establishment of a PM roadmap for policy makers as well as other specific scientific goals.

- PerMediNA’s Vision

Responding to the challenge of implementing PM in NA, PerMediNA was developed through substantial funds over two years from the MEAE under the FSPI program (Fond de Solidarité pour les Projets de l’Innovation).

Through the PerMediNA project we seek to build a comprehensive ecosystem where stakeholders such as clinicians, advocacy groups, patients, data curators, biotech companies, policy makers, funders and pharmaceutical companies alongside with other partners mainly involved in Ethical, Legal, and Social Implications (ELSI), contribute together to shape the future of healthcare. By harnessing the collective expertise and resources of its diverse stakeholders, PerMediNA aims to not only advance scientific knowledge but also to drive transformative progress in PM practice while addressing broader societal and ethical considerations in the North African region

- Goals

The project goals cover a wide range of key areas related to PM with the intent to establish collaborative networks of North African researchers pursuing genomics-based, disease-oriented projects and create or expand infrastructure for genomic medicine research that would enable scientists in NA to handle large cohorts, generate data sets and increase the capacity to analyze them.

PerMediNA specific goals include:

- 1) Assessment and description of PM readiness level in NA.
- 2) Set-up a pilot project on precision oncology which will constitute the backbone of the PerMediNA initiative.
- 3) Initiation and training activities on PM in NA. The program includes training activities to build a sustainable critical mass of researchers, medical doctors and data curators in NA.
- 4) Drafting a clear roadmap with recommendations for policy makers on the implementation of PM in NA.
- 5) Building an effective North African PM ecosystem
- 6) Communication, outreach, dissemination, valorisation and sustainability are also among the main goals of the PerMediNA project.

In addition to these specific goals, a particular attention is paid to gender equity in the PerMediNA consortium. Therefore, the gender dimension has been taken into consideration in the selection of cohorts for sequencing as well as in the selection of participants who will benefit from the training activities. We also aim to ensure that both women and men can benefit equally and fairly from healthcare services, in terms of prevention, diagnosis and personalized treatment. Involving as many young researchers as possible into the different activities of the project is another key goal of the PerMediNA initiative. In this context, some activities will be carried out exclusively by young researchers. Young scientists will also be prioritized to participate in the training courses organized in the framework of the project. We also plan to train future trainers, who will be considered as referees in their respective

institutions for knowledge transfer and for the sustainability of the various activities of the project.

Methodology

The PerMediNA initiative includes 4 main work packages designed to achieve the project’s goals: 1) Situation Analysis and inventory of existing PM means; 2) Pilot project on precision oncology; 3) Training, Dissemination & Communication; 4) Implementation & sustainability.

Situation analysis and inventory of existing PM means

The readiness level assessment aims to provide a concrete and updated state of the art of PM implementation in NA. Through a multidimensional approach, interviews with Key Opinion Leaders, focus groups, surveys and questionnaires have been used to collect information of the readiness level of PM in the region. s. The used methodology is outlined in Fig. 2.

Pilot project on precision oncology: a case study on lung cancer

In the framework of this project, a total of 450 Non-Small Cell Lung Cancer (NSCLC) cases (150 from each of the three participating countries) were collected with all associated phenotypic and clinicopathological data. Genomic and transcriptomic data from WES, large gene panels and RNA sequencing (RNASeq) will be generated locally and in collaboration with the Biomics NGS core facility in Paris (Fig. 3). A total of 100 adjacent normal tissues from the same samples will be also analyzed in order to appropriately perform RNAseq data analysis and be able to conduct differential gene expression analysis.

Tailored bioinformatics pipelines have been developed using suitable tools to efficiently process, analyze and integrate the large-scale raw data that will be generated in the frame of this project based on the type of technology used. Raw data generated from DNA sequencing will be processed to identify genomic variants using toolkits such as Genome Analysis Toolkit (GATK) [32] and Mutect2 [33]. In parallel with the genomic analysis, transcriptomics investigation will be conducted on the raw data generated through RNA sequencing. This will help to identify differentially expressed genes (DEGs), allele specific expression, long non-coding RNAs, genetic variants and gene fusions. Appropriate bioinformatics tools will be used for gene fusions and SNPs detection such as STAR-Fusion, Fusion Finder, Arriba [34] as well as

GATK [35].

Functional annotation of detected variants will be performed using multiple software tools including Annovar [36], SnpEff [37], SnpSift [37], Variant Effect Predictor (VEP) and Variant Annotation and Filter Tool (Varaft) [38]. Results will be combined to optimally select the most relevant variants involved in disease development, prognosis and therapeutic options along with their associated biological processes and metabolic pathways.

In addition, multi-omics data available in public databases (dbSNP, HGMD GO, KEGG...) and in the literature will be integrated for a better understanding of the underlying mechanisms linked to LC. Actionable variants, known to have a clinical impact will be identified and the phenotype-genotype correlations will be discussed and communicated to oncologists. Integrative multi-omics data approaches will be combined with data science and machine learning approaches to predict genetic biomarkers for better diagnosis and to estimate the timelines for comprehensive genetic testing needed to treat this malignancy. Finally, novel variants and variants with conflicting interpretations of their pathogenicity will be studied in vitro using genome editing and CRISPR-cas technology.

Training, dissemination and communication

In the framework of this project, several training activities have been organized focusing on different topics related to precision medicine from ethics and regulations to data analysis, biobanking, interpretation and functional validation. This includes the organization of courses, workshops, and internships in partner institutes to consolidate knowledge and skills.

Dissemination and communication on the project and its progress have been achieved through continuous updates to the project’s website, publications on social networks including twitter, facebook, youtube and twitter, and also press releases.

To evaluate and measure the achievements of project goals, specific, measurable and time-bound key performance indicators were fixed including results metrics and impact scores. An evaluation and monitoring process is also used to follow these metrics regularly.

Results and main achievements

The PerMediNA consortium offers an excellent environment to facilitate the implementation of PM in the North African region and to



Fig. 1. Description of PerMediNA consortium partners.

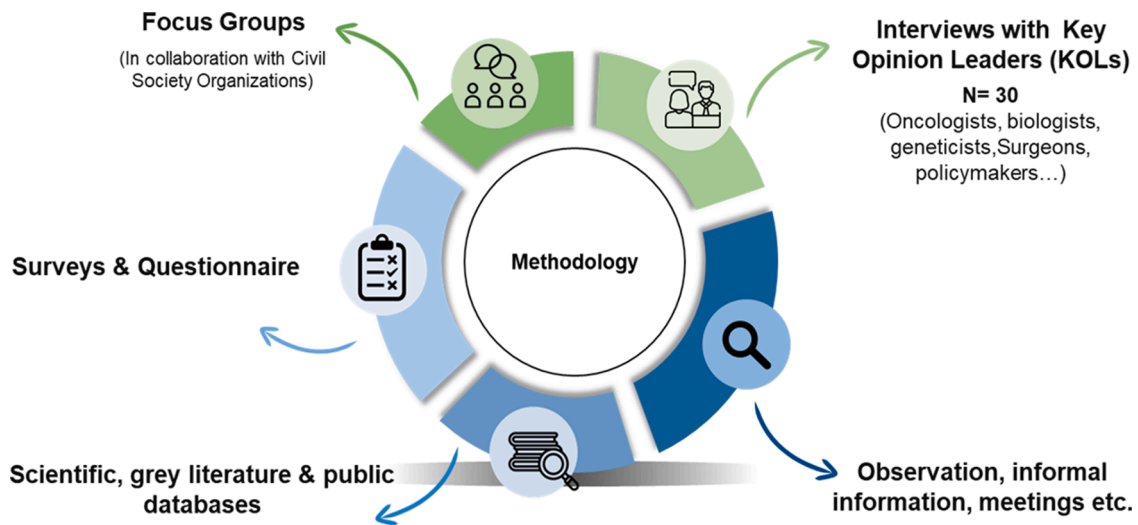


Fig. 2. Methodology used to assess the Readiness Level for PM implementation.

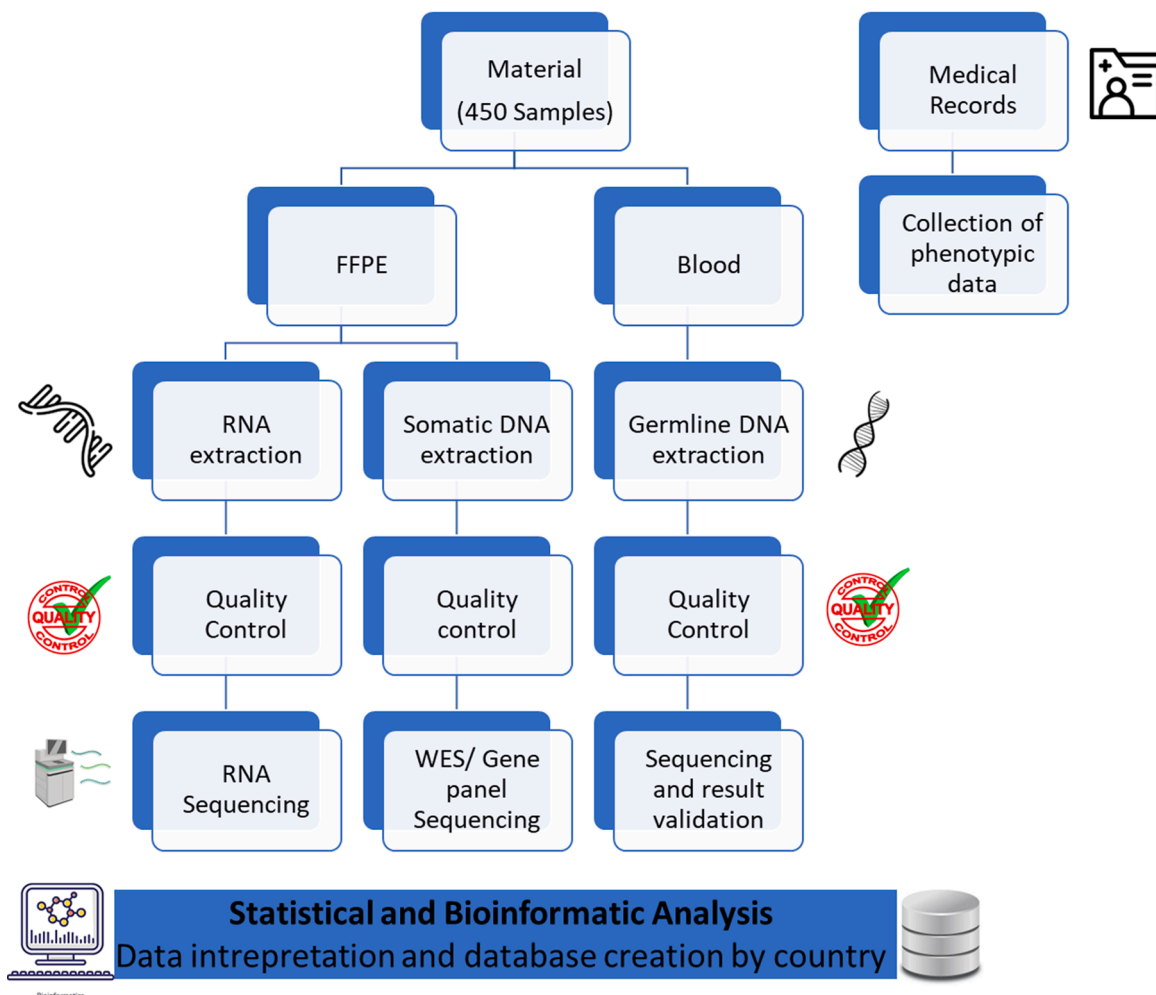


Fig. 3. Methodology used for sample collection and Data Analysis.

help scientists to develop their research capacities in the field of PM.. This is achieved by taking advantage of existing resources in the different participating sites combined with the capacities that have been put in place in the framework of the project.

Readiness level assessment

The assessment of the readiness level (Fig. 4) for PM implementation has been performed in the three participating countries (Tunisia, Morocco, Algeria) through:

- * Identification of all stakeholders involved in the precision medicine field across the three countries.
- * Identification and data curation of all scientific publications and gray literature related to PM in NA in order to establish a comprehensive knowledge base of the PM in NA.
- * Collection of OMICs data and identification of all related public databases.
- * Assessment of existing infrastructure needed for effective PM implementation (Next Generation sequencing (NGS) platforms, biobanks, functional genomics platforms, and Electronic Health Records (EHR)).
- * Mapping of the existing ethics committees and gathering information on the regulations and laws related to biomedical research which will provide the necessary framework for responsible and compliant research practice.
- * Identification of patients' needs such as medical requirements, social and psychological care through collaboration with patient support groups and associations.

PM development also requires building on existing cohorts, data, infrastructure and developed genomic medicine research. Indeed, the PerMediNA initiative took advantage of previous projects and is in interaction with other ongoing ones. These ongoing projects are related to genomics medicine and biomedical fields and involve more than 25 institutions from 15 African countries in addition to more than 15 American, European and Canadian institutions. The main previous and ongoing projects are illustrated in [Supplementary Figure 1](#) and detailed in [Supplementary Table 1](#).

In addition, a targeted curriculum was developed within the Biomics core facility and the Bioinformatics and Biostatistics Hub from Institut Pasteur Paris to address specific needs on the use of genomics sequencing platforms and bioinformatic analysis and interpretation of data derived from the PerMediNA initiative.

Training and capacity building activities

Several theoretical courses and workshops on PM-related topics have been organized ([Fig. 5](#)).

- Implementation-Research Course

A course on Implementation Research was organized in collaboration with the World Health organisation Regional Training centre. This Regional training center is based at Institut Pasteur de Tunis and supported by the Special Programme for Research and Training in Tropical Diseases (TDR). This course focused on how to design and demonstrate robust implementation research projects to improve control of diseases and generate better health outcomes in countries with limited resources.

During this course, ethical issues related to research projects were also raised. The goal is to understand the main success criterias for the implementation of PM.

- Precision Medicine Academy

The Precision Medicine Academy (PMA) was organized by the Institut Pasteur de Tunis. The PMA included a series of lectures and practical training sessions led by recognized experts in the field of PM.

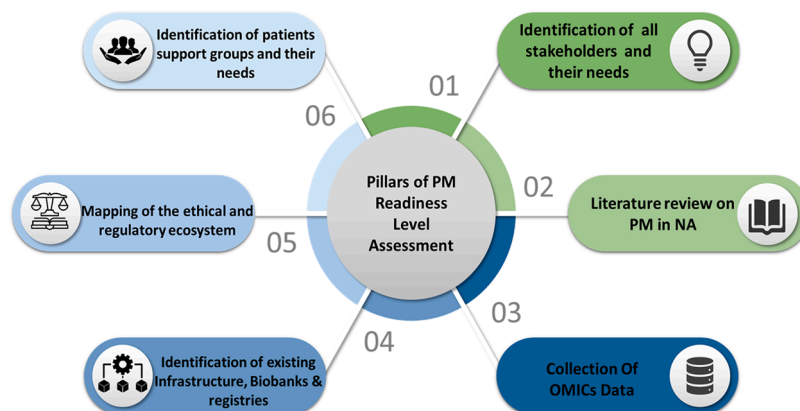
This PMA was led in two phases:

The first part of this event was dedicated to theoretical courses on PM. Leading scientists, computational biology researchers and clinicians presented captivating lectures, covering a wide range of topics from the molecular basis of the disease to ethical and regulatory aspects related to PM application. The fruitful exchanges between participants and trainers helped consolidate the theoretical skills needed to integrate PM into their practices.

The second part of the PMA offered participants an opportunity to acquire practical skills related to the analysis of human complex genomic data. Indeed, a **workshop on OMICs data analysis** was organized involving 20 participants from the three Pasteur Institutes. This workshop was animated by experts from the Bioinformatics and Biostatistics Hub at Institut Pasteur Paris and facilitated by trainers and experts from Institut Pasteur de Tunis. Participants gained new insights in OMICs data analysis, including common procedures used to perform calling of genetic variants and genotyping and were guided step by step in analyzing and interpreting high throughput data from data pre-processing and quality control until variant annotation and filtering. Participants were also divided into four different working groups and worked on the following projects: Variant Calling of somatic variants from Whole Exome Sequencing (WES) data, Structural Variants Analysis tools, benchmarking of variant calling pipelines and variant calling using Freebays. Alongside the hands-on training, a session dedicated to Molecular Tumor Boards (MTBs) has also been organized. This key training opportunity focused on communication and collaboration between clinicians and researchers to tackle complex cases, interpret patients data and develop personalized treatment plans.

- Internships

To further support the human capacity building, several scholarships were allocated, offering trainees the opportunity to undertake internships within partner institutes, notably the Bioinformatics and Biostatistics Hub and the Biomics NGS (Next Generation Sequencing) core facility [39] at Institut Pasteur Paris and IGR ([Fig. 5](#)). The aim of these internships is to enable trainees to reinforce their knowledge and skills from data generation to functional validation. Indeed, the internship in the Biomics NGS core facility covered NGS workflow from library



. 4. The six pillars of PM readiness level assessment.

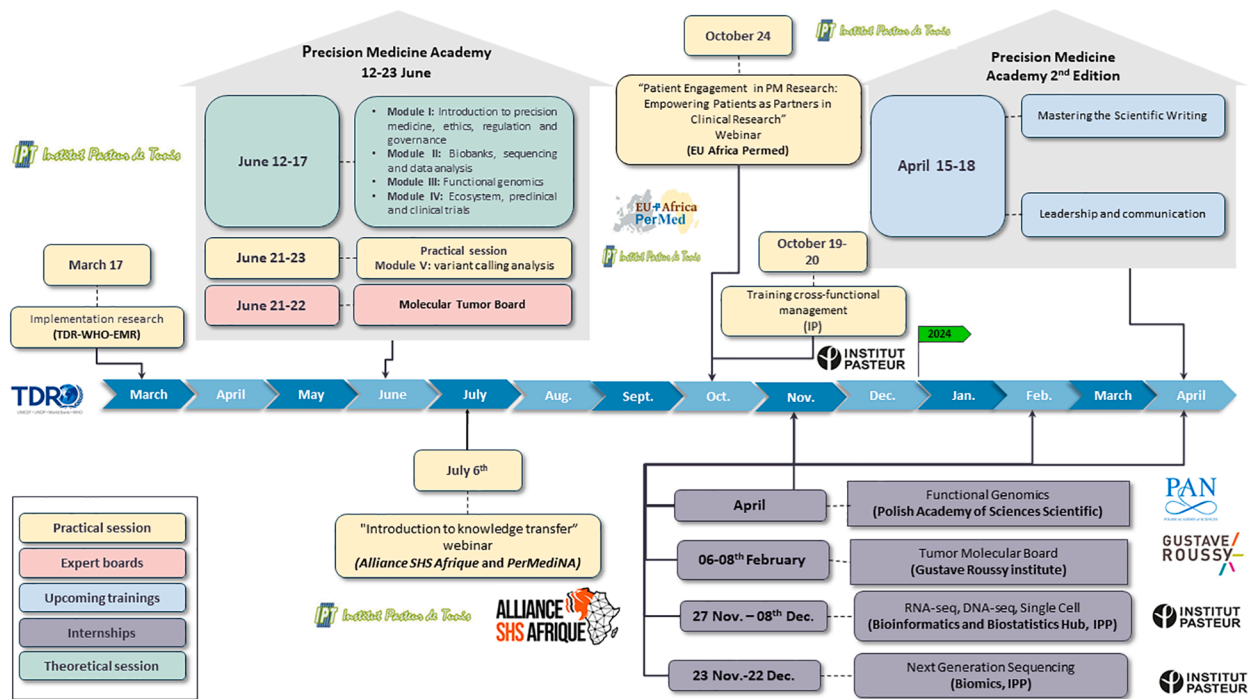


Fig. 5. The training programs of the PerMediNA project.

preparation to primary quality control of the generated data. Meanwhile, the training on OMICs data analysis included advanced bioinformatic modules including RNAseq bulk, single cell, gene fusion prediction, DNAseq as well as biological interpretation of data. The internship in IGR covered aspects related to Molecular Tumor Boards.

Pilot project on precision oncology

A pilot project on Precision Oncology, particularly on Non-Small Cell Lung Cancer (NSCLC) is being conducted in the frame of this initiative. This is achieved through strengthening the capacities in terms of wet lab small equipment, reagents, kits, and consumables for NGS library preparation and sequencing as well as computing infrastructure within the three Pasteur Institutes involved in the project, which will enable to broaden the spectrum of PM services in partnerships with oncologists, pharmaceutical and biotechnology companies.

Indeed, several high-throughput sequencing platforms are available in the participating countries, including: an Illumina NextSeq 550 platform at Charles Nicolle Hospital in Tunisia, an Illumina NextSeq 1000, an iSeq 100 and a MinION mk1b nanopore platforms at the Institut Pasteur de Tunis, two Illumina MiSeq, a Thermo Fisher Ion GeneStudio S5 System and three MinION Mk1c platforms at the Institut Pasteur d'Algérie and a MiSeq platform at the Mustapha University Hospital Center as well as an illumina NextSeq 2000, an illumina MiSeq and Nanopore MinION Sequencer at the genomic sequencing center of Institut Pasteur du Maroc.

Extensive efforts have been made by the investigators in the three Pasteur institutes to establish a robust network of oncologists, surgeons and pathologists for the collection of samples and phenotypic data of more than 450 NSCLC cases. In Tunisia, a synergistic collaboration has been put in place with oncologists and pathologists at the Abderrahman Mami Hospital, which is the reference center for lung diseases. Genomic and transcriptomic data from WES, large gene panels and RNASeq will be generated for a total of 450 NSCLC samples using NGS platforms.

Molecular tumor boards and genome editing task forces

In the PerMediNA project, two Task forces of significant impact have been put in place and are dedicated to implementing MTBs and functional genomics.

During the PMA, a workshop on MTBs was organized at Institut Pasteur de Tunis and was led by experts from the IGR. The aim of this workshop was to familiarize participants with the context of MTBs and to facilitate establishing these meetings in Tunisia. This workshop was followed by the implementation of a task force on MTBs in Institut Pasteur de Tunis that focuses on bringing together multidisciplinary teams of Tunisian healthcare professionals (oncologists, surgeons, pathologists, cytogeneticists, biologists) to discuss and strategize the most effective treatment plans for cancer patients. The collaboration between Tunisian healthcare professionals from diverse backgrounds, coupled with the involvement of French experts from the IGR following the PMA training, sets the stage for a comprehensive approach to cancer care and marks a groundbreaking initiative in NA.

On the other hand, a functional genomics task force was put in place in collaboration with the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences focusing mainly on genome editing technologies especially the CRISPR-Cas systems. This technology will be used to assess the functional effect of the relevant novel variants identified in this project and to discover novel therapeutic options.

Additionally, molecular analyses, such as RNA sequencing and/or qPCR, may be employed to demonstrate the altered gene expression changes introduced by the CRISPR-mediated gene editing (Fig. 6).

Building precision medicine ecosystem

This project operates within a dynamic precision medicine ecosystem, spanning multiple sites and disciplines. It involves a diverse range of stakeholders including academic and non-academic partners like biotech partners and pharma companies in addition to other actors (Supplementary Figure 2) which helps in developing new products that can be used in the field of genomic medicine such as specific gene panels or PanelApps.

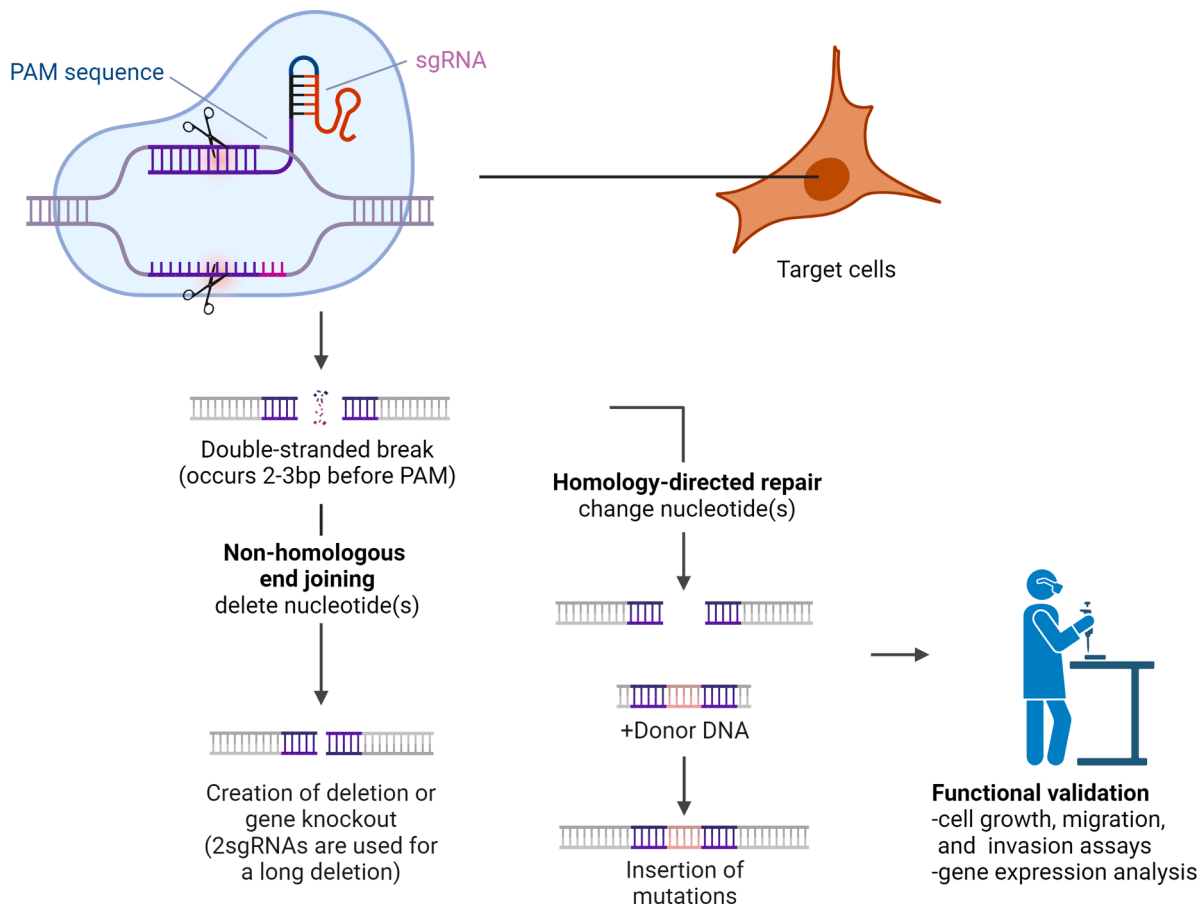


Fig. 6. The CRISPR-Cas gene editing technique that will be used for functional assays in the framework of the PerMediNA project. This figure was created using BioRender.com.

Communication and outreach

The main goal of the communication activities is to reach and inform a wide audience. These actions increase the project's visibility and support all stakeholders to identify concrete partnership opportunities. The success of the dissemination and communication activities is ensured through the strong collaborations and networks that the consortium members have with various regional, and international institutions.

Considering the scope of the PerMediNA project and its target audience, the dissemination activities consisted of continuous updating of the project's website, publications and participation in international events and conferences. The digital communication was supported by social media (Supplementary Figure 3) (Twitter, LinkedIn, Youtube and Facebook) to ensure the development of communities around the initiative. The key project meetings, events and findings have benefited from stronger outreach tools, including press and media communication. Due to the impactful statistics of our social media (Supplementary Figure 3), new collaborations with existing networks and consortia are being established (EU-Africa PerMed, IC PerMed, etc.)

Discussion and futures directions

Several efforts are being undertaken by the members of the PerMediNA initiative to ensure an effective implementation of PM in the region taking into account challenges specific to the North African context. It is noteworthy that for an effective implementation of PM it is important to build on existing cohorts, data, infrastructure, and prior genomic medicine research initiatives. In fact, the PerMediNA project has capitalized on past projects and is actively engaging with other

ongoing initiatives in the field. The outcomes of the readiness level assessment, the situational analysis, as well as any identified gaps and challenges, will be comprehensively documented in a strategic report. This report will be disseminated to share the valuable experiences of each participating country with others worldwide.

Advancing the field of precision oncology in North Africa

Findings of this project will improve our knowledge on the molecular profile LC and will help to identify novel therapeutic targets. In addition, and by taking into account the main output of PM which is a better overall treatment decision that better meets patients' needs with fewer negative consequences, we aim to translate these research findings into health products and services by putting in place cost effective, affordable and sustainable genetic testing for cancer patients. This project will help to develop good practice and share experiences for the implementation of future genetic and molecular analysis dedicated to PM.

Enhanced human capacity building

Even though large-scale efforts have been made to address several challenges faced in the whole life cycle of PM, additional efforts are still needed to train all stakeholders in the development of new analysis methods, new technologies, new biological directions, data science, drug discovery, ethics and regulations. In the framework of this project, several courses, workshops and internships were organized with plans for additional training activities to enhance capacity building and improve knowledge and skills of young researchers, medical staff and other stakeholders that may play a key role in PM implementation (Fig. 5). Within this project, we have also placed a specific focus on

enhancing data generation and analysis capabilities as well as facilitating information sharing. Indeed, with the introduction of novel high throughput technologies, the access to data has become easier. In NA, while expertise and skills have been developed, a small amount of data has been generated so far. This gap in data generation acts as both a challenge and an opportunity. We therefore aspire to establish a North African hub of scientific excellence for establishing PM in current healthcare.

At Institut Pasteur de Tunis, we are committed to further enhancing the expertise of key stakeholders involved in the implementation of PM. To this end, we will host a second edition of the PMA event, featuring extensive training sessions on scientific writing, communication, and soft skills. The scientific writing workshop will be mainly dedicated to clinicians to strengthen their critical thinking and scientific writing abilities in compliance to high standards and to promote clinicians' engagement in the research field. The soft skills workshop aims to enhance participants' capacities in communication and leadership. Through interactive sessions, role-playing, and discussions, the workshop will help to equip participants with the tools to communicate persuasively when presenting their scientific findings and also with the required skills to effectively lead and manage their teams. In addition, Institut Pasteur d'Algérie is planning to organize training sessions of two days on PM application in LC while Institut Pasteur du Maroc is set to conduct a two days workshop on PM implementation as well. Other planned training sessions will be organized on MTBs, bioinformatics data analysis and RNA sequencing and metagenomics and this latter will be in collaboration with the Biomics NGS core facility team from Institut Pasteur Paris. In addition an internship on Functional genomics is planned at the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences and will be focused on the implementation and testing of functional assays such as the CRISPR-cas technology that will be used to assess the functional impact of the relevant variants identified in the framework of this project. Indeed, by introducing specific variations into the desired gene, we will be able to confirm the functional impact of variants and their role in disease development [40]. Moreover, using this same technology and by knocking out genes found to be overexpressed in tumor tissues and observing the resulting phenotypic changes that affect disease progression, we may identify novel genes that might be considered as potential therapeutic targets [41]. Functional validation of pathogenic cancer mutations found in NGS using several molecular tools, including CRISPR-Cas, will allow us to confirm the importance of genetic changes in cancer-development-related processes [42,43].

Establishment of PerMedina consortium

One of the main goals of the PerMediNA initiative is to develop a strategy for implementing and strengthening PM in the North African region in collaboration with the involved professionals and national authorities. Thanks to the strong collaborative links between all members of the current initiative as well as the complementarities of their research directions and their recognized expertise, a unique multidisciplinary research environment is established in the framework of this project under a cooperative environment of partnership and trust. Therefore, a North African PM consortium in collaboration with our partners in France is under creation and it will employ North African institutes' scope of experts across a wide range of specialties, which will ensure the smooth running of the consortium, its sustainability and skills transfer in Africa and outside. This multidisciplinary core is represented by researchers, clinicians, pathologists, pharmaceutical and biotechnology partners, heads of health care departments, bioinformaticians, data curators and decision makers working together to deliver an impactful PM research for the well-being of the North African populations. In addition, this initiative aims to focus on implementing technological advancements, efficient pipelines, facilitating knowledge transfer, fostering connections between existing research facilities and providing

training for young clinicians and scientists to seamlessly integrate PM in their routine practice and research activities.

Validate a roadmap for PM implementation in North Africa

There is a growing sense across the North African scientific community that the time has come to articulate a vision for the next phase of Data-driven Decision Programs and to accelerate progress in moving from translational research to medicine practice [44]. In the framework of this project, we will establish a strategy and a roadmap to help decision makers achieve efficient and cost effective PM implementation in NA, by identifying challenges and opportunities at the national and regional levels and by establishing common and/or specific strategies depending on the real settings of each country involved in the current project. In Tunisia, the ministry of Health is currently working on a national plan for PM implementation in close collaboration with the Tunisian Ministry of Higher education and Scientific Research and Tunisian Experts in the field of PM.

This roadmap will be validated by the scientific advisory board with key opinion leaders and it will be based on:

- A Situation Analysis: the assessment of the readiness level that will be performed in the framework of this project.
- A Gap Analysis to identify the major challenges that need to be overcome.
- A SWOT analysis to identify the Strengths, Weaknesses, Opportunities and threats of the PM approach that are specific to the North African countries.
- Drafting and publishing the recommendations and the roadmap in a policy brief that will be shared with Policy and decision makers from the North African countries.
- Follow up on the effective implementation and application of the suggested recommendations.

This roadmap will ultimately be used to translate research findings into translational medicine practice for other cancers, other diseases and other African countries or Low and Middle Income Countries (LMICs) including the evaluation of the effectiveness and reliability of the different methods.

Sustainability plan and interaction with other permed consortia

The multidisciplinary core of the PerMediNA consortium constitutes an excellent scientific and professional environment. To ensure the smooth running of this initiative and its sustainability, scientific and info-days will be organized to inform on the progress of the project and to define its short-, mid- and long-term goals. During these events, socio-economic partners, funding agencies and policy makers will be invited to raise awareness of the importance of funding PM related projects to guarantee the sustainability of the project activities. In the meantime, members of the group will have the opportunity to participate in events organized by the International Consortium for PM (IC PerMed), as well as the "Africa EU-PerMed" Consortium, and the European Alliance of Personalized Medicine which will help consolidate regional and international efforts for the implementation of PM in each of the participating countries (Fig. 7).

In collaboration with the Grant Office of Institut Pasteur de Tunis, a monitoring system for new financing opportunities will be used to identify and submit new projects, and raise more funding to guarantee the sustainability of the project and the consortium.

Moreover, the PerMediNA consortium is willing to establish South-South Collaboration with SubSaharan African countries for a mutual exchange of experience and knowledge. Indeed, some members from the PerMediNA project are active members of the H3Africa consortium and worked all together with other subSaharan African scientists to develop a framework on the implementation of Genomic Medicine in Africa [44,

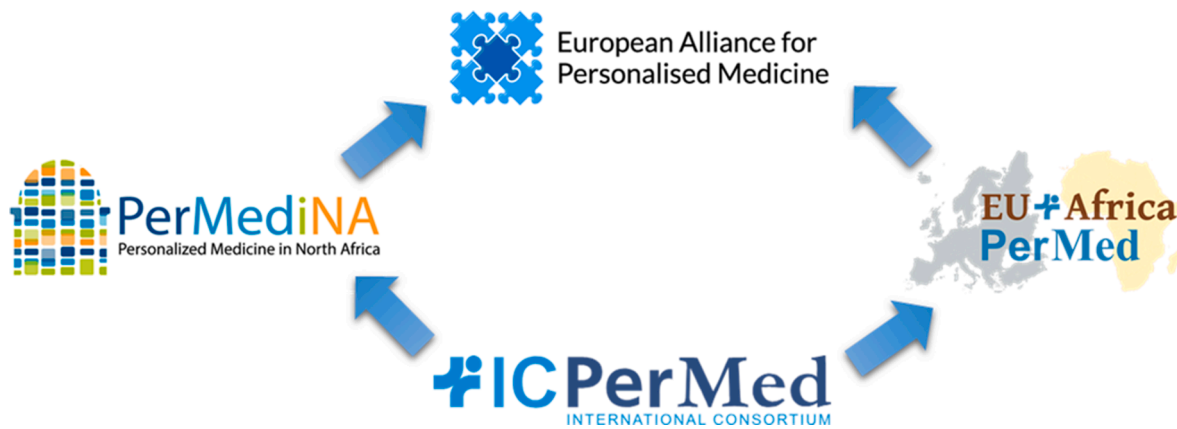


Fig. 7. Interaction between PerMediNA and other International initiatives and Consortia on personalized medicine.

45], which has been adopted and published by the African Academy of Sciences (AAS) and the African Union Development Agency (AUDA).

Conclusion

The implementation of PM represents a significant leap forward in healthcare, promising personalized and targeted treatment strategies and contributing to more cost-effective interventions. However, most of the PM related work on the African continent is currently being done in a research context. Throughout this project, we aim to start translating innovative research findings into healthcare services and products in order to enable greater precision in disease prevention, diagnosis and treatment by educating consumers and providers, accelerating research and supporting necessary changes in policy and regulation. Although much of the PM-related studies in North African countries is currently performed in a research setting, our project has endeavored to bridge the gap between research and clinical settings using innovative and translational approaches.

Ethics approval and consent to participate

Not Applicable

Availability of data and materials

Not applicable

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Author contribution

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing, others, who have contributed in other ways should be listed as contributors.

CRedit authorship contribution statement

Yosr Hamdi: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Maroua Boujemaa:** Writing – review & editing, Visualization, Methodology. **Jihenne Ben Aissa-Hajj:** Writing – review & editing, Visualization. **Fouzia Radouani:** Writing – review & editing, Investigation. **Meriem Khyatti:** Writing – review &

editing, Investigation. **Najah Mighri:** Writing – review & editing, Investigation. **Mariem Hannachi:** Writing – review & editing, Visualization. **Kais Ghedira:** Writing – review & editing. **Oussema Souiai:** Writing – review & editing. **Chaïma Hkimi:** Writing – review & editing, Visualization. **Mohamed Selim Kammoun:** Writing – review & editing, Methodology. **Nesrine Mejri:** Resources. **Hanen Bouaziz:** Resources. **Mohamed Amine Beloufa:** Writing – review & editing. **Hicham Charoute:** Writing – review & editing. **Abdelhamid Barakat:** Writing – review & editing. **Imène Najjar:** Writing – review & editing. **Hiroaki Taniguchi:** Writing – review & editing, Visualization. **Natalia Pietrosevoli:** Writing – review & editing. **Koussay Dellagi:** Writing – review & editing. **Sonia Abdelhak:** Writing – review & editing. **Mohamed Samir Boubaker:** Writing – review & editing. **Claudia Chica:** Writing – review & editing. **Etienne Rouleau:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.tranon.2024.101940](https://doi.org/10.1016/j.tranon.2024.101940).

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