



NEWROAD

Drug Discovery Platform

User Manual

EU4Health Programme EU4H-2021-PJ2-16
Action grants for the Computer-aided Drug Repurposing for Cancer Therapy Project
GA No: 101080024

27 October 2023



**Co-funded by
the European Union**

Project Acronym:	NEWROAD
Project Full Name:	Open Platform for European Networking and Repurposing of Oncological Assets and Drugs
Grant Agreement #	101080024
Work Package	WP1
Task	Deliverable D1.2
Document Name:	User Manual for NEWROAD Drug Discovery Platform
Nature (R, P, D, O) ¹	R
Dissemination Level (PU, PP, RE, CO) ²	PU
Document Reference:	UNISA-NRD-D1.2
Version / Submission	v0.3 / Oct 27 2023
Editor:	Simona Concilio
Institution:	University of Salerno
E-Mail:	sconcilio@unisa.it

Abstract

The NEWROAD Drug Discovery Platform Manual is a comprehensive resource designed to facilitate user understanding and utilization of this powerful platform. This manual consists of multiple sections, each dedicated to a distinct aspect of the platform's functionality. Users will find step-by-step instructions for various tasks, ranging from setting up access credentials to configuring jobs, employing computational tools, and evaluating results. To ensure ongoing relevance and utility, this manual is regularly updated on an annual basis or less as needed.

Keywords

User Manual, Drug Discovery Software, In Silico Analysis, Drug Repurposing, Data Sharing, [...]

MODIFICATION CONTROL			
Version	Date	Status	Author (s)
0.1	25/10/2023	Draft	Dr Simona Concilio Dr Francesco Marrafino
0.2	26/10/2023	Draft	Dr Vassilis Virvilis Dr Eftychia Lekka Dr Andreas Persidis
0.3	27/10/2023	Final ver. of deliverable D1.2	Dr Francesco Marrafino

¹ R=Report, P=Prototype, D=Demonstrator, O=Other

² PU=Public, PP=Restricted to other programme participants (including the Commission Services), RE=Restricted to a group specified by the consortium (including the Commission Services), CO=Confidential, only for members of the consortium (including the Commission Services)

Table of Contents

1. Introduction	4
1.1 About NEWROAD	4
1.2 Primary Users	4
1.3 Access and Permissions	5
2. NEWROAD Visual Explorer	6
2.1 Literature Search Module	6
3. Molecule and Protein Target Visualization	9
3.1 Exploring Structural Aspects	9
3.2 Protein Interaction Analysis	9
4. Calculations	11
4.1 Job Setup	11
4.2 Molecular Similarity	11
4.3 Identification of Allosteric Sites	12
4.4 Affinity Prediction	12
4.5 Metabolic Modifications	12
4.6 Chemical Stability	12
4.7 Lead Optimization	13
4.8 Repurposing of Drugs	13
5. Semantic Analysis	14
6. Automatic Reporting	15
7. Collaborative Login and Space Management	16
8. Support and Help	17
8.1 Accessing the Knowledge Base	17
8.2 Contacting Support	17

1. INTRODUCTION

The NEWROAD platform, an integral part of the European Union-funded NEWROAD project, co-funded by the European Union, is an innovative and collaborative in silico tool designed for systematic drug repurposing in the field of oncology. This platform is tailored for researchers, drug discovery scientists, and clinicians in the life sciences domain. Its primary purpose is to empower users to identify novel therapies with a high degree of predictive accuracy, initially focusing on rare and paediatric cancer research.

More info at: <https://new-road.eu/>

Note: This user manual is for reference purposes and is based on the information available during the pre-alpha stage of the NEWROAD platform. For the most up-to-date information and assistance, please refer to the official platform documentation and support channels. An updated version of the manual will be released along with the NEWROAD platform operational prototype.

1.1 About NEWROAD

The NEWROAD project is a significant endeavour aimed at establishing a European-wide capability for Systematic Drug Repurposing (SDR). This capability allows for the identification of promising therapeutic options for various diseases, with a focus on oncology. NEWROAD is built on an Augmented Intelligence (Aul) architecture layered upon Artificial Intelligence (AI) algorithms. It enables the repurposing of drugs for specific diseases or combinations of diseases. The key functions of the NEWROAD platform are as follows:

1. **Development of Novel Therapies:** The platform's primary function is the repurposing of drugs, initially targeting oncology. It identifies and assesses the potential of existing compounds for new therapeutic purposes.
2. **Sharing Clinical Data:** NEWROAD facilitates the sharing of clinical data among entities in the European Community. This sharing is essential for research collaboration and informed decision-making.
3. **Open Collaborative Platform:** NEWROAD serves as an open and collaborative platform for Systematic Drug Repurposing. It encourages researchers to engage, collaborate, and contribute their expertise to advance drug discovery efforts.

1.2 Primary Users

The NEWROAD platform is designed for individuals with a background in life sciences, including researchers, drug discovery scientists, and clinicians. It caters to those seeking to identify and explore new therapeutic options, especially in the

context of rare and paediatric cancers. Users of the platform are expected to have a strong foundation in life sciences and an interest in drug repurposing.

1.3 Access and Permissions

Access to the NEWROAD platform is not granted autonomously. Users must request access, which will be reviewed and approved by the NEWROAD Consortium or management team. This validation process is essential due to the sensitive data handled by the platform. Depending on the nature of your work and your role, you may be granted different levels of access and permissions within the platform. Users can:

- **Register:** Registration and login to the platform will be granted upon request and approval.
- **Create Workspaces:** Users can create dedicated workspaces for their organizations, each with its own administrators and users with varying levels of permissions.
- **Collaborate:** Users can collaborate with other authorized users, sharing data and workspace resources.
- The NEWROAD platform's access and permissions system ensures that sensitive data is protected, and that collaboration is controlled and secure.

In the following sections of this manual, you will learn how to navigate the NEWROAD platform, make the most of its features, and engage in systematic drug repurposing in the field of oncology. Whether you're searching scientific literature, visualizing molecules, and protein targets, performing various calculations, or managing your collaborative workspace, this user manual will provide you with step-by-step instructions to maximize your research capabilities.

Keep in mind that the platform is in the pre-alpha stage, and features may evolve over time. Your feedback and contributions are highly valuable in shaping the future of the NEWROAD platform. We invite you to explore and utilize the platform's potential, working collectively toward improved therapeutic options for cancer and beyond.

2. NEWROAD VISUAL EXPLORER

The NEWROAD platform offers a dedicated tool named **NEWROAD Visual Explorer**, which is based on Biovista Vizit, a visual bibliographic PubMed-based search tool. The tool helps biomedical researchers and medical practitioners explore the biology of a biomedical domain [e.g., a disease, a drug, or an Adverse Event (AE) of interest], discover non-obvious links between biomedical terms (e.g., drugs, AEs, diseases, genes, biological processes, cell types), visualize biological interconnections and communicate findings with peers.

Core to the NEWROAD Visual Explorer is the capability to fuse different data sets and overlay their results in a comprehensive and easy to navigate way. The **NEWROAD Visual Explorer** enables users to access and explore both scientific literature and structural-related data, creating networks to find connections between the elements being analysed.

2.1 Literature Search Module

The Literature Search capability of the **NEWROAD Visual Explorer** provides an innovative way to access scientific literature. When you type in a search term, you'll be presented with a visual network of related terms, eliminating the need to sift through extensive lists of publication titles. This tool streamlines the process of finding specific studies of interest, enhancing your research efficiency.

The **Literature Search** module uses over 16 different Knowledge Sources (Ontologies and Controlled Vocabularies) as the starting material in order to generate a search space in the form of biomedical term lists. In addition to the publicly available Resources, Biovista compiles additional controlled vocabularies and ontologies in-house.

The biomedical entity/term types represented in the Literature Search module, include:

- Genes (from >2000 different organisms, including organisms in the Human Microbiome Project)
- Biological Processes (Pathways)
- Diseases (Medical Conditions)
- Adverse Events
- Drugs (Small molecules, Biologics with Pharmacological action)
- Compounds
- Lipids
- Human Microbiome Project Reference organisms (> 2000 species)
- Cell Lines

The Literature Search module gives scientists and medical professionals a new way of using the literature to advance their work.

- With the Literature Search module, when users type in a search term, instead of a list of publications, they get a visual network of related terms.
- Literature Search module users no longer need to shift through long lists of paper titles to find the ones they want.
- Literature Search module users can also save the networks they create. And they can share their insights with their peers.

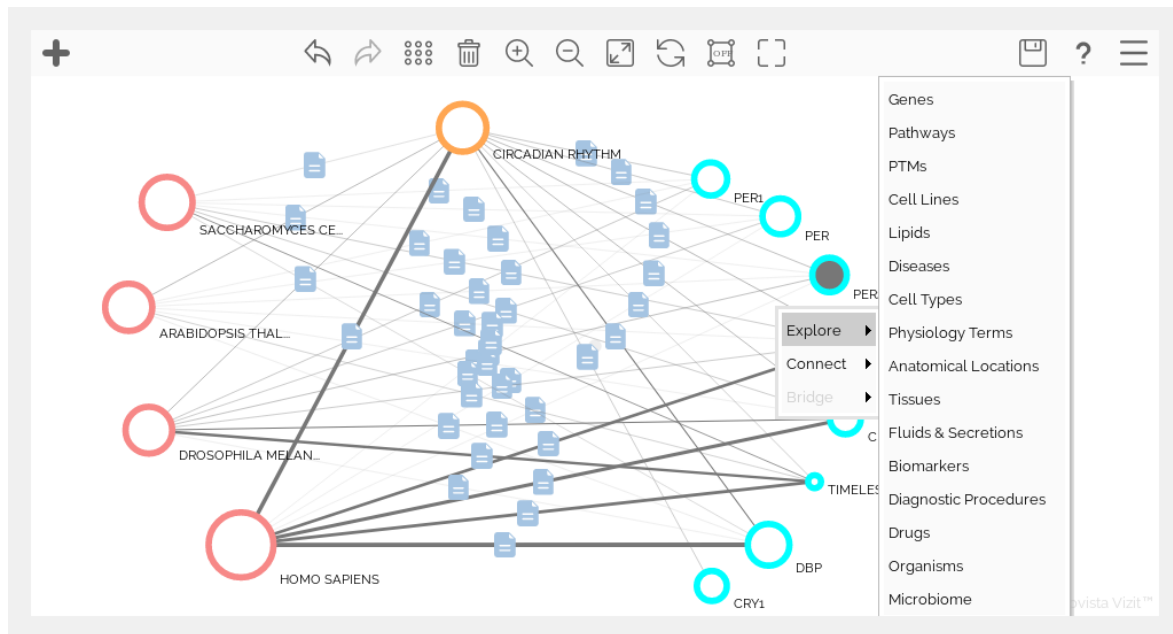


Figure 1: A Literature Search module Graph

With the Literature Search module one can search graphs of relationships between concepts of interest such as genes, diseases, compounds, and cell types to obtain an overview of the knowledge that is captured in scientific literature (PubMed/MEDLINE). It is then one easy step to drill down to the underlying literature and explore these relationships in depth.

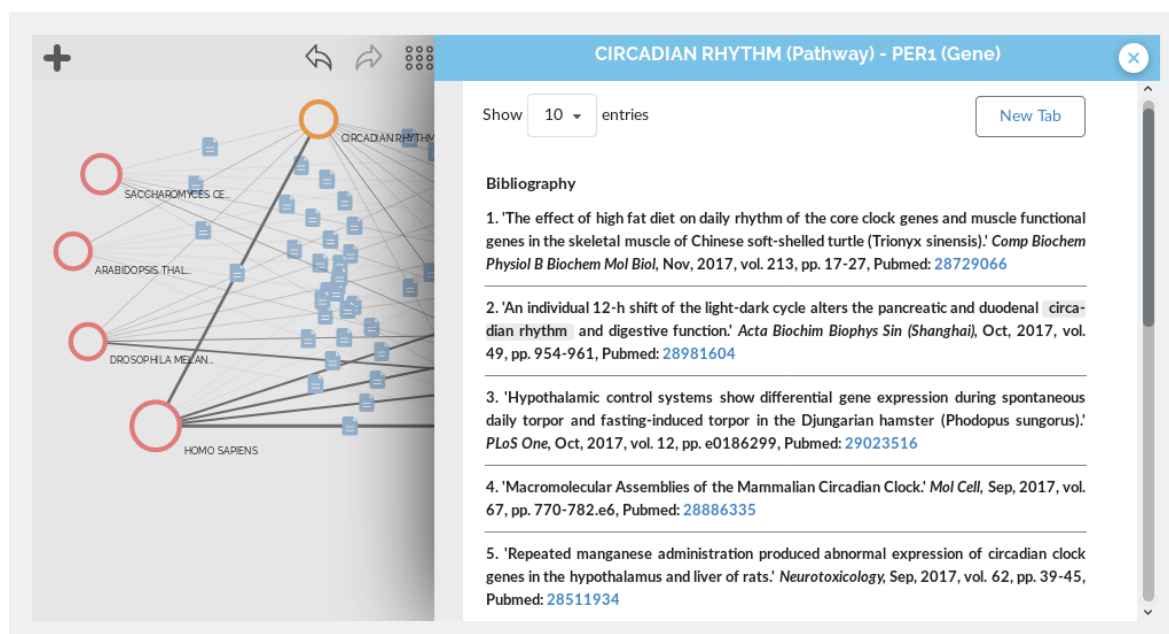


Figure 2: Literature Search Supporting Evidence

Literature Search allows users to search, understand, discover, capture, organize and share knowledge in a single, easy to use environment.

Key features of the Literature Search module:

- **Visual Network:** Instead of traditional text-based search results, users are presented with a visual network of related terms, such as genes, diseases, compounds, and cell types. This network gives you an overview of the knowledge captured in scientific literature.
- **Save Networks:** Users have the ability to save the networks they create, facilitating easy reference and access to relevant studies.
- **Share Insights:** Collaborate with your peers by sharing the networks you've created. This feature promotes knowledge sharing and teamwork within the research community.

To use the Literature Search module effectively, follow these steps:

1. Access the Literature Search module within the platform's interface.
2. Enter your search term or query of interest.
3. Explore the visual network of related terms to identify relevant studies and connections.
4. Save networks for future reference if you wish.
5. Share your insights and findings with colleagues or collaborators to promote collaborative research.

This feature empowers researchers to harness the wealth of scientific literature for advancing their work in drug repurposing. The Literature Search Tool simplifies the process of finding and accessing relevant studies, saving you time, and ensuring that your research is well-informed.

3. MOLECULE AND PROTEIN TARGET VISUALIZATION

The NEWROAD platform offers powerful tools for visualizing molecules and protein targets. This section outlines the key features and functions related to molecule and protein target visualization.

3.1 Exploring Structural Aspects

Molecule and protein visualization within the NEWROAD platform serve as a crucial element for understanding the structural aspects of compounds and their interactions with biological targets.

Key Functions:

- **Visual Exploration:** The platform allows users to explore 3D representations of molecules and their interaction with target proteins.
- **Structural Insights:** Gain a deeper understanding of the physical and chemical properties of compounds and the specific regions where they interact with target proteins.
- **Visualization Tools:** The platform provides a range of visualization tools and controls to manipulate and analyse molecular structures effectively.

To effectively utilize this feature, follow these steps:

1. Access the Molecule and Protein Visualization section within the platform.
2. Select the molecule or protein target of interest.
3. Utilize the provided visualization tools to explore the structural aspects, such as 3D representations.
4. Analyse the interaction between molecules and their target proteins, identifying critical structural elements.

This feature empowers researchers to gain valuable insights into the structural aspects of compounds and protein interactions, which is essential for making informed decisions in the drug repurposing process.

3.2 Protein Interaction Analysis

In addition to visualizing structural aspects, the NEWROAD platform offers tools for analysing protein interactions.

Key Functions:

- **Protein Interaction Networks:** Explore the networks of protein-protein interactions related to your research.
- **Functional Insights:** Gain insights into the functional relationships and associations between proteins.

- **Data Visualization:** Utilize charts and graphs to interpret protein interaction data effectively.

To make the most of this feature, follow these steps:

1. Navigate to the Protein Interaction Analysis section within the platform.
2. Select the proteins of interest or query specific interactions.
3. Explore the resulting protein interaction networks.
4. Analyse the functional insights and use data visualization tools to enhance your understanding.

This feature allows researchers to uncover critical protein interactions and functional relationships. In the following sections of this user manual, you will explore additional capabilities of the NEWROAD platform. These include calculations, semantic analysis, automatic reporting, and collaborative space management. Each of these features is designed to support and enhance your research efforts in systematic drug repurposing.

4. CALCULATIONS

The NEWROAD platform offers a diverse array of calculations for systematic drug repurposing. These calculations encompass various aspects crucial for the identification, evaluation, and optimization of potential drug candidates. Available calculations are based on SoftMining Proprietary algorithms. In this section, we will provide a detailed overview of each type of calculation available within the platform.

4.1 Job Setup

Before diving into the specifics of each calculation type, it's important to understand how to set up a job within the NEWROAD platform. A "job" represents a specific task or analysis you want to perform. The platform allows you to configure and initiate jobs based on your research needs.

Key Functions:

- **Job Configuration:** Specify the parameters and inputs required for the analysis.
- **Data Input:** You can either manually input parameters or upload a "parameter file" to initiate a job.
- **Progress Monitoring:** The platform provides real-time monitoring of job progress.

To set up a job, follow these general steps:

1. Access the **Job Setup** section within the platform.
2. Configure the job by specifying the parameters required for the analysis. You can input these manually or upload a preconfigured "parameter file."
3. Initiate the job, and the platform will commence the analysis.
4. Monitor the real-time progress of the job to ensure it is running as intended.

4.2 Molecular Similarity

Molecular similarity calculations allow users to compare a selected molecule with other compounds to identify structurally similar molecules that could be potential repurposing candidates. To execute a molecular similarity job:

1. Load the molecule of interest.
2. Set up a **Molecular Similarity** job specifying the parameters for the calculation, including similarity thresholds and comparison criteria.
3. Initiate the job to search for similar molecules.

4.3 Identification of Allosteric Sites

Allosteric sites identification allows users to find potential allosteric binding site within the selected target(s). This process involves pinpointing regulatory regions within proteins. To execute an allosteric site identification job:

1. Load the target protein of interest.
2. Run a file preparation job if necessary to ensure the protein is in the correct format.
3. Execute the **Allosteric Site Identification** job to locate regulatory regions within the protein.

4.4 Affinity Prediction

Affinity prediction calculations allow to assess the binding affinity of compounds to target proteins. This prediction is crucial for identifying potential repurposing candidates with high binding affinities. To execute an affinity prediction job:

1. Load the target protein and the ligand or a panel of ligands you wish to evaluate.
2. Configure the **Affinity Prediction** job parameters, specifying the calculation method and criteria for affinity prediction.
3. Initiate the job to predict the binding affinities.

4.5 ADMET Properties

Assessing the ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties of compounds is crucial for determining whether the compound is suitable for repurposing and if it exhibits the desired pharmacological characteristics for the intended therapeutic use. To execute an ADMET properties assessment:

1. Load the molecule or compound you wish to assess for its ADMET properties.
2. Configure the job parameters, specifying the specific ADMET properties you want to investigate.
3. Initiate the job to evaluate the ADMET properties of the compound.

4.6 Metabolic Modifications

Metabolic modifications calculations allow to explore how compounds are metabolically processed within biological systems. To execute a metabolic modification job:

1. Load the molecule you want to investigate.
2. Run the **Metabolic Modification** calculation to explore the metabolic modifications of the compound within the biological system.

4.7 Chemical Stability

Chemical stability analysis ensures that repurposing candidates remain stable and effective in their new context. To execute a chemical stability job:

1. Load the molecule or compound you want to assess.

2. Configure the **Chemical Stability** job with the appropriate parameters for stability analysis.
3. Initiate the job to assess the chemical stability of the compound.

4.7 Lead Optimization

Lead optimization calculations are designed to refine and select the most promising repurposing candidates. This process involves analysing structure-activity relationships (SAR) and conducting lead optimization calculations. To execute a lead optimization job:

1. Load the molecule or compound of interest.
2. Set up the **Lead Optimization** job with the desired parameters.
3. Initiate the job to optimize lead compounds for repurposing objectives.

4.8 Drug Repurposing

The core function of the NEWROAD platform is to support the repurposing of existing drugs. This calculation type allows researchers to analyse available drugs and assess their potential for repurposing in the context of oncology. To execute a drug repurposing job:

1. Load the target protein and the ligand or panel of ligands you wish to evaluate.
2. Configure the **Repurposing** job parameters, specifying criteria and methods for repurposing assessment.
3. Initiate the job to identify potential drug candidates/targets.

Each type of calculation within the NEWROAD platform serves a unique purpose in the systematic drug repurposing process. The platform's calculation capabilities are designed to empower researchers and support the identification of novel therapies in the field of oncology.

Please note that additional information regarding the process, including instructions on launching jobs, visualizing, exploring, and exporting results, will be made available in the updated version of the manual. This updated manual will be provided upon the release of the first operational prototype of the platform.

5. SEMANTIC ANALYSIS

Powered by SoftMining proprietary algorithms, semantic analysis is a crucial component integrated into various algorithms and processes within the NEWROAD platform. It enhances the interpretation of data and aids in the identification of potential drug candidates. Users do not need to have specialized knowledge of semantic analysis to benefit from this feature. Instead, it operates seamlessly within the platform's algorithms to improve data comprehension and knowledge extraction.

Semantic analysis enhances the following aspects of the NEWROAD platform:

- **Data Interpretation:** By incorporating semantic analysis, the platform can interpret and understand data in a more context-aware manner. This helps researchers in identifying subtle connections and patterns that might not be immediately evident.
- **Conceptual Relationships:** The platform leverages semantic analysis to recognize conceptual relationships between genes, diseases, compounds, and other data points. This facilitates a deeper understanding of the data's significance.
- **Data Integration:** Semantic analysis contributes to the effective integration of disparate data sources. It aligns data with a common understanding, making it easier to correlate information from various domains.
- **Pattern Recognition:** Semantic analysis supports the recognition of patterns and associations within complex datasets, helping researchers pinpoint potential repurposing candidates and insights.

Semantic analysis is a behind-the-scenes feature that significantly enhances the platform's capabilities. It assists in making data more accessible and actionable, allowing users to make informed decisions in their drug repurposing efforts.

6. AUTOMATIC REPORTING

The NEWROAD platform streamlines the reporting process by automating the creation of reports. This feature ensures that researchers can communicate their repurposing candidates and strategies efficiently.

Key functions of the Automatic Reporting feature:

- **Report Generation:** The platform automatically compiles data and analysis results into comprehensive reports.
- **Customization:** Users can customize report templates to include specific data points and insights that are most relevant to their research.
- **Accessibility:** Generated reports can be easily accessed and shared with collaborators or stakeholders.

To generate automatic reports, follow these steps:

1. Navigate to the **Automatic Reporting** section within the platform.
2. Select the job or analysis for which you want to generate a report.
3. Customize the report template, specifying the information and data you wish to include.
4. Initiate the report generation process, and the platform will compile the report based on your selections.

Automatic reporting simplifies the task of documenting research findings, making it easier to communicate your repurposing candidates and strategies to peers and stakeholders.

7. COLLABORATIVE LOGIN AND SPACE MANAGEMENT

The collaborative login and space management system within the NEWROAD platform fosters an environment for users to work together, share data, and collaborate seamlessly. This feature is designed to enhance user engagement and promote effective teamwork.

Key functionalities of collaborative login and space management:

- **User Authentication:** Users can securely log in and access their dedicated spaces within the platform.
- **Workspace Creation:** Users have the ability to create dedicated workspaces for their organizations. These workspaces can be configured to meet specific research and collaboration needs.
- **User Permissions:** The platform allows for the assignment of different levels of access and permissions to users within workspaces. This ensures that data and resources are protected while facilitating collaboration.
- **Data Sharing:** Users can share their work with authorized colleagues, both within and outside their organizations. Sharing can be controlled to ensure data privacy and security.

The collaborative login and space management system enables researchers to work collaboratively, manage their workspace efficiently, and share data and insights with the appropriate stakeholders. It serves as the foundation for teamwork and knowledge exchange within the NEWROAD platform.

8. SUPPORT AND HELP

Accessing support and help resources is essential to make the most of the NEWROAD platform. In this section, we'll explore how users can access the knowledge base and contact support when needed.

8.1 Accessing the Knowledge Base

The knowledge base is a valuable resource within the NEWROAD platform, providing a repository of information, guides, and documentation to assist users. It serves as a reference hub for gaining insights into platform features and best practices in systematic drug repurposing.

Key features of the knowledge base:

- **Comprehensive Guides:** Access detailed guides, manuals, and tutorials related to platform functionalities, calculations, and data interpretation.
- **Frequently Asked Questions (FAQs):** Browse a collection of frequently asked questions and their answers to address common queries.
- **Video Tutorials:** Explore video tutorials that provide step-by-step instructions on using specific features or conducting calculations.

To access the knowledge base, follow these steps:

1. Log in to the NEWROAD platform using your credentials.
2. Navigate to the "Knowledge Base" section, typically located within the user dashboard, or help menu.
3. Browse and search for relevant articles, guides, or videos to find the information you need.

The knowledge base is a valuable self-help resource designed to empower users with the knowledge and guidance necessary for effective utilization of the platform's capabilities.

8.2 Contacting Support

While the knowledge base provides a wealth of information, there may be instances where users require additional assistance or have specific questions or issues. The platform offers a support system to address these needs.

Key features of the support system:

- **Contact Channels:** Users can reach out to support through various contact channels, including email, chat, or a dedicated support portal.
- **Issue Resolution:** The support team is available to assist users in resolving technical or platform-related issues.

- **User Guidance:** Support can provide guidance on best practices, platform usage, and help address user concerns.

To contact support, follow these steps:

1. Access the "Contact Support" section within the NEWROAD platform.
2. Select the preferred contact channel (e.g., email, chat, or support portal).
3. Describe the issue, question, or request in detail.
4. Submit your inquiry, and the support team will respond promptly to provide assistance.

Contacting support ensures that users receive timely and personalized guidance when facing challenges or uncertainties while using the platform. The support team is dedicated to helping users make the most of the NEWROAD platform and its features.

As you explore the platform and engage in systematic drug repurposing within the field of oncology, the support and help resources are invaluable for enhancing your experience and ensuring productive research outcomes.