# LYSOCIL Project

## Excel in Rare Diseases' Research: Focus on LYSOsomal Disorders and CILiopathies

Deliverable 7.2 Project website launch and Visual Identity Guide

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## Table of Contents

## 1. Overview

This document is developed as part of the project "*Excel in Rare Diseases' Research: Focus on LYSOsomal Disorders and CILiopathies*" (hereinafter referred as LYSOCIL) which has received funding from the European Union's H2020-TWINN-2017, under the Grant Agreement 811087. This report is developed under the scope of the **WP7 Dissemination and Communication**.

WP7 will support the project's implementation with the main objective of communicating and disseminating information about RDs and in particular lysosomal and ciliary disorders, to ensure the highest possible impact across and beyond the consortium. An integrated set of dissemination and communication activities will raise awareness on the project's activities and outputs among its key targets. The dissemination and communication activities will address, in a personalised manner, the needs of the different targeted stakeholders and end-users of the project.

## 2. Creation of the LYSOCIL Logo

The LYSOCIL project aims to address the current need for a scientific strategy to reinforce research and innovation excellence in the study of lysosomal diseases and ciliopathies, with special attention to the diagnosis and etiology of these diseases.

The Chronic Diseases Research Center of NOVA Medical School (UNL-NMS-CEDOC) aims to be at the forefront of European and international scientific excellence in chronic rare diseases. For that, the institute is twinning with Münster University (WWU) and Telethon Institute of Genetics and Medicine (FTELE.IGM) to create and integrated network of interactions to power the research capacity of UNL-NMS-CEDOC and of its local and national systems.

For the graphic identity of the LYSOCIL project, there is a need to convey that it is a "brand" connected to the health sector, focused on the investigation of lysosomal diseases and ciliopathies.

*Fig. 1 - Inspiration images for the LYSOCIL logo*

The creative agency took inspiration from petri dishes (Fig. 1). The main proposal revolved around the vision through a microscope of a sample on a petri dish, forming the word LYSOCIL. The letters are irregular, creating movement, to resemble a real sample (Fig. 2).

The blue color is connected to the color of UNL-NMS-CEDOC logo, in order to create a connection to the mother-brand but transmitting a lighter more positive image, with a lighter shade (Fig. 3).


*Fig. 2 - First main logo proposal*


*Fig. 3 - Other proposals for the LYSOCIL logo*

The logo suggestions were presented to the consortium during the LYSOCIL Kick-off meeting, on December 3rd and 4th. A quick survey showed an overall preference for the main proposal, though it was decided thatit still needed some adjustments. As such, the group agreed to ask the company developing the logo for new suggestions base on the preferred logo.

The creative agency was asked to turn the logo more abstract, as it was too literal, and it resembled lysosomes too much. Based on the preferred proposal, 3 other proposals were created (Fig. 4).


*Fig. 4 - Second logo proposal*

After consulting with the members of the Consortium, we established the logo for the LYSOCIL project (Fig. 5).


*Fig. 5 - Official logo of the LYSOCIL project*

## 3. Creation of the LYSOCIL Website

The LYSOCIL website is divided in two parts, one aimed for public consultation and a Research HUB, restricted to the participants of the project, to exchange information on grant opportunities, interesting papers, conferences, etc.

It was decided that the website would have three top tabs, "*About LYSOCIL*", "*News*" and "*Events*", and four main tabs, "*Lysosomal diseases*", "*Ciliopathies*", "*Help & Support*" and "*Research*".

The top tabs are focused mainly on the LYOSCIL project itself. The "*About LYSOCIL*" tab showcases the main objectives of the project and explains the choice to cover rare diseases, mainly lysosomal disorders and ciliopathies. In this tab, it is also possible to learn more about the institutions involved in the LYSOCIL project, including UNL-NMS-CEDOC, WWU and FTELE.IGM. The "*News*" and "*Events*" tabs cover the latest news and the forthcoming workshops, conferences, etc., to happen under the scope of the project.

As the website is directed more towards the general public, the main tabs are mainly focused on rare diseases. On the "*Lysosomal diseases*" and "*Ciliopathies*" tabs it is explained, in a more simplified manner, what these disorders are, the main symptoms, diagnosis and their main cause.

For the "*Help & Support*" tab the main focus is people with symptoms of a rare disease and/or people diagnosed with a rare disease. This tab aims to inform people on what to do when you or someone you know has a rare disease or suspects having (where to go for information, tests, counselling, etc.), with additional information for people with an already a diagnosis regarding help and support lines, such as *Linha Rara*, the support line of *Raríssimas*, and other useful communities and resources.

Lastly, the "*Research*" tab gathers all the information regarding on-going research on rare diseases, mainly lysosomal disorders and ciliopathies, as well as milestones on diagnosis and treatments, with a language for lay people.

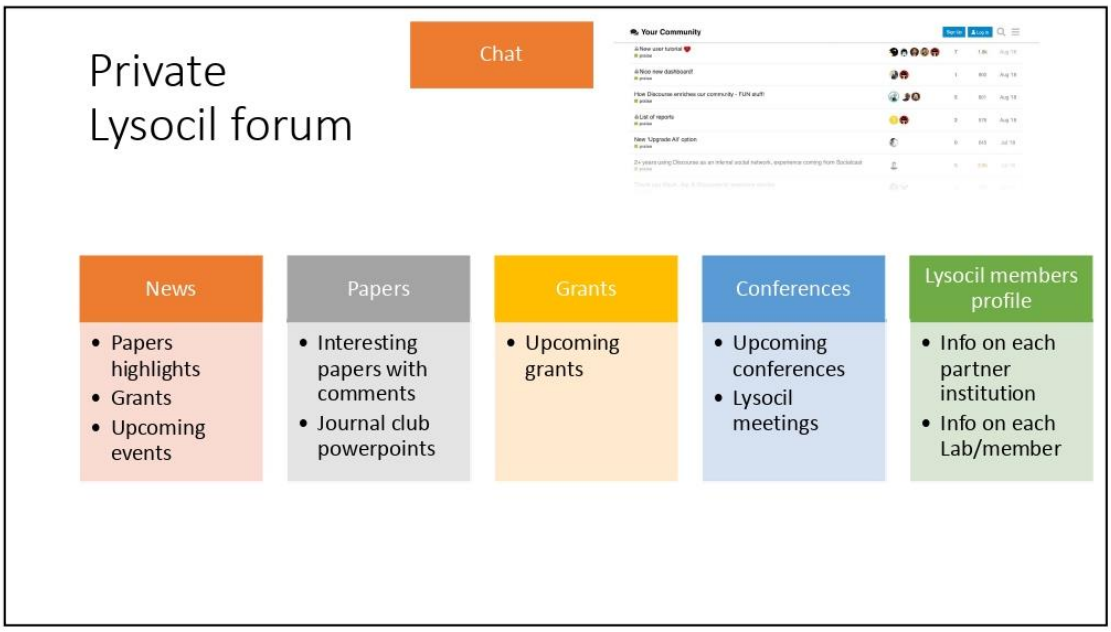
Listed as the main contact point for the LYSOCIL project is the LYSOCIL management email account: manage.lysocil@nms.unl.pt.

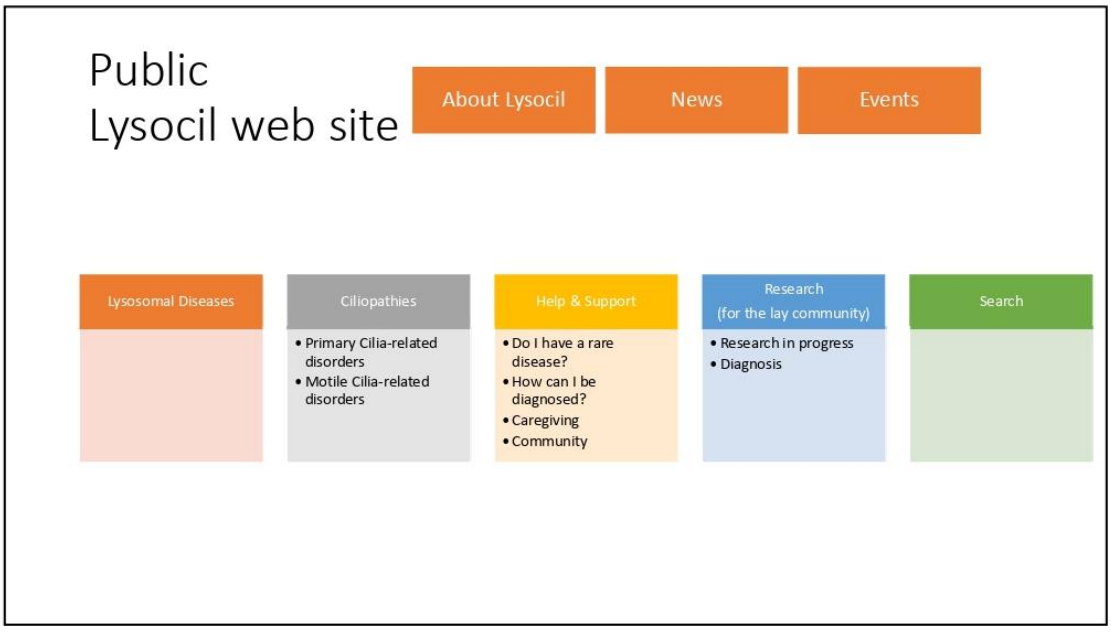
The design and production of the LYSOCIL website are being developed by the creative company and the finished product will be uploaded on the next Communication and Promotional Materials deliverable.

In Annex 1 and 2 is the website's structure and contents, respectively.

# Annexes

## 1. LYSOCIL website's structure



**2. LYSOCIL website's content**

# [ABOUT LYSOCIL]

**LYSOCIL: Excel in Rare Diseases' Research: Focus on LYSOsomal Disorders and CILiopathies** is a Twinning Project led by NOVA Medical School (NMS) that aims to strengthen the research and innovation capacity of the Chronic Diseases Research Center (CEDOC), helping it to become a national and internationally-recognized Centre of Excellence in chronic rare diseases research and innovation.

For this project, CEDOC partnered up with two international-leading institutions, Münster University (WWU), a German institution with a strong research profile in basic, clinical and translational medicine connected to rare diseases, and Telethon Institute of Genetics and Medicine (TIGEM), the leading Italian research center dedicated to understanding the molecular mechanisms behind rare genetic diseases.

This partnership will boost the multidisciplinary knowledge and experience, as well as research and training practices and widen the collaborative networks to step up the excellence of the research of the involved partners.

## WHY RARE DISEASES?

Rare diseases (RD) represent a big challenge for biomedical research, healthcare and society in general, given their high diversity and low numbers/scattered distribution of patients.

Even though the incidence of each rare disease is not higher than 1 in 2,000 newborns, there are around 7,000 RDs that affect 30 million people in Europe alone. In Portugal, it is estimated that 600-800,000 people suffer from RDs.

In most cases, diagnosis is especially difficult for these diseases, the drugs that are available are expensive and the interest of the pharmaceutical industry in developing new drugs is limited, all this leading to patients and their families lacking satisfying answers.

Lysosomal diseases and ciliopathies are conditions that share the same basic molecular defect(s) and common defective cellular phenotypes, despite being clinically very diverse. These are two of the main research fields of CEDOC, and the ones subject to strengthening through this Twinning project.

## PARTNER INSTITUTIONS

**CEDOC (Portugal)**

CEDOC [link to CEDOC website] is located at the heart of NOVA Medical School (NMS) and is affiliated with 10 Hospitals in the Lisbon Metro area. CEDCO-NMS also has established protocols with several patient associations (APDP – Protective Association of Diabetics of Portugal, and Raríssimas) and Medical Societies (e.g. Portuguese Society for Rheumatology).

Created in 2007, CEDOC-NMS brings together biomedical, translational and clinical research under a multidisciplinary and collaborative spirit, hosting a strong scientific critical mass with the mission of better understanding the molecular mechanisms of chronic diseases and develop advanced and personalized therapies, which ultimately lead to an improvement in the quality of life and well-being of the population.

[Google maps Widget]

**Münster University (Germany)**

Munster University (WWU) [link to website] is the fifth-largest University in Germany. The Medical Faculty of WWU aims to connect excellent basic science and clinical science focusing on immediate translation of new basic knowledge into clinical research and innovative practical patient care, diagnosis and treatment for the sake of patient's health.

The Department of General Pediatrics of the Medical Faculty of WWU has a strong interest in rare diseases, both with regard to clinical care and basic and translational research. The main research focus of the Department are ciliopathies, such as Primary Ciliary Dyskinesia (PCD), metabolic diseases, and pediatric syndromic and renal diseases, often associated with cilia dysfunction.

[Google maps Widget]

**Telethon Institute of Genetics and Medicine (Italy)**

Telethon Institute of Genetics and Medicine (TIGEM) [link to website] is a Telethon Foundation organization founded in 1994 as a leading Italian research center, located in Pozzuoli, Italy, just outside Naples.

TIGEM is a multidisciplinary research institute devoted to the study of the mechanisms underlying rare genetic diseases and to the development of innovative therapies. The main research focus of this institute are neurodegenerative diseases, lysosomal storage disorders, membrane trafficking defects, disorders of liver metabolism and eye diseases.

[Google maps Widget]

# [NEWS]

## LYSOCIL KICK-OFF MEETING

Marking the launch of the LYSOCIL project, the kick-off meeting was held on December 3rd and 4th 2018, bringing together members of the partner institutions and the external advisory board.

# [EVENTS]

Announcing the next activity/event

# [LYSOSOMAL DISEASES]

Lysosomes are vesicles that contain digestive enzymes which can break down different kinds of macromolecules. Lysosomes are also involved in various cell processes, including secretion, plasma membrane repair, cell signaling and energy metabolism.

Lysosomes are known to contain more than 60 different enzymes and have more than 50 membrane proteins. Mutations in the genes that encode any of these proteins can cause a genetic disorder.

Lysosome-related organelles (LROs) share features with lysosomes. However, they contain specialized cargo and are present in specialized cells. Examples are melanosomes from melanocytes and platelet dense granules. Dysfunction in these organelles is associated with several rare diseases.

**Lysosomal-Storage Disorders (LSDs):**
Group of rare and recessively-inherited metabolic dysfunctions with an overall incidence of 1/5,000. LSDs often show a multisystemic phenotype associated with severe neurodegeneration, mental decline, cognitive problems and behavioral abnormalities. Other tissues commonly affected are bone and muscle.

LSDs are caused by mutations in genes that affect lysosomal function, leading to the abnormal build-up of various toxic materials in the cells, ultimately resulting in tissue/organ dysfunction.

**Griscelli Syndrome (GS):**
Divided in three sub-types: GS1, GS2 and GS3, according with the mutated disease-causing-gene. All forms of GS present hypopigmentation of the hair and skin, immunological defects and in the case of GS2 also immune dysfunction.

At the molecular level, GS entails defects in the compartments of a complex that allows melanosomes to be transferred from melanocytes to keratinocytes, where they protect nuclear DNA from ultraviolet radiation.

**Hermansky-Pudlak Syndrome (HPS):**
Multisystem, heterogeneous genetic disorder characterized by a combination of albinism and bleeding diathesis.

This disorder is caused by mutations in 8 different genes, which lead to a deficient production of melanin in melanocytes and platelet dense granules.

**Choroideremia:**
Genetic disorder of retinal degeneration that usually affects males. Female carriers may have mild symptoms without loss of vision. The rate and degree of vision loss differs among individuals.

This rare X-linked disorder can be caused by many different mutations in a gene involved in vesicle trafficking within retinal cells.

## [CILIOPATHIES]

Cilia are microscopic, finger-like projections that stick out from the surface of cells and are involved in sensing the physical environment and chemical signaling. Motile and non-motile cilia are present in almost all cells and their dysfunction causes diseases known as ciliopathies.

The number of reported ciliopathies (currently 35) is increasing, as is the number of established (187) and candidate (241) ciliopathy-associated genes.

**Primary Ciliary Dyskinesia (PCD):**
Congenital heterogeneous disorder with an estimated prevalence of 1:10,000, which is higher in consanguineous populations. As many patients are believed to remain undiagnosed, it is thought that the correct prevalence of the disease is still unknown.

This disorder leads to chronic respiratory infections, usually beginning at birth with respiratory distress followed by a wet cough in early childhood and evolving to include bronchiectasis and chronic sinusitis. The earlier it is diagnosed, the better prognosis the patients will have.

As half the PCD cases are associated with *situs inversus* and heterotaxy, this disorder is not just respiratory and can have a high correlation with congenital heart disease. Male sterility is also common in adults, since sperm flagella are motile cilia and may also present defective motility.

PCD is characterized by a deficient mucociliary clearance, which is caused by one or several factors, such as lack of motile cilia, uncoordinated ciliary pattern or total lack of ciliary motion. This disorder usually follows an autosomal recessive heritance pattern, with more than 40 genes found to cause it when mutated.

**Polycystic Kidney Disease (PKD):**
Genetic disorder in which the renal tubules become structurally abnormal, resulting in the development and growth of multiple cysts within the kidney.

**Joubert Syndrome:**
Disorder of brain development that affects many parts of the body, characterized by the absence or underdevelopment of the part of the brain that controls balance and coordination (cerebellar vermis) and a malformed brain stem.

This syndrome can be caused by mutations in more than 30 genes, which affect the structure and function of cilia, leading to disruptions of important signaling pathways during development.

**Asphyxiating thoracic dystrophy (Jeune Syndrome):**
Hereditary disorder of bone growth characterized by a narrow chest, short ribs, shortened bones in the arms and legs, short stature, and extra fingers and toes (polydactyly).

At least 11 genes have been found to cause this syndrome. Mutations in these genes disrupt the normal assembly or function of cilia, leading to missing or abnormal cilia in many types of cells.

**Bardet-Biedl Syndrome:**
Disorder characterized by loss of vision, obesity, the presence of extra fingers or toes (polydactyly), intellectual disability or learning problems, and abnormalities of the genitalia.

This syndrome can result from mutations in at least 14 different genes, which cause defects in the structure and function of cilia, disrupting important signaling pathways during development and lead to abnormalities of sensory perception.

# [HELP & SUPPORT]

## DO I HAVE A RARE DISEASE?

- Symptoms?
- Family history?

## I HAVE A RARE DISEASE

- Symptoms?
- Diagnosis?
- Next steps

## CAREGIVING

## COMMUNITY

Raríssimas

Aliança Portuguesa de Associações de Doenças Raras

## RESOURCES

Raríssimas – Associação Nacional de Deficiências Mentais e Raras

Linha rara – 300 505 700 | linharara@rarissimas.pt

# [RESEARCH]

## RESEARCH IN PROGRESS

[Recent papers relating to the disorders in focus]

## MILESTONES

[Important milestones on research]

## DIAGNOSIS

### Lysosomal Diseases

**Lysosomal-Storage Disorders (LSDs):**
The clinical presentation of LSDs depends on the type, quantity and site of storage of undegraded material. However there are a number of overlapping clinical features that are not specific for LSDs, which can make the diagnosis very challenging. The diagnosis for LSDs is established by specific enzyme assays, through urine analysis for specific undegraded macromolecules, and mutational analysis.

Prenatal diagnosis is possible for all lysosomal storage disorders.

**Griscelli Syndrome (GS):**
The diagnosis of GC is usually supported by the microscopy examination of the hair shaft. The characteristic neurological symptoms and analysis of lymphocyte cytotoxic activity of patients tend to discriminate the molecular causes. Confirmation can be provided by mutation analysis of the patient's DNA.

Direct mutation-based carrier detection and prenatal diagnosis are possible in families with defined gene mutations.

**Hermansky-Pudlak Syndrome (HPS):**
HPS is diagnosed through clinical features, such as hypopigmentation of the skin and hair, characteristic eye findings and characteristic appearance of platelets under an electron microscope.
Molecular genetic testing for mutations in the *HPS1*, *AP3B1*, *HPS3*, *HPS4*, *HPS5*, *HPS6*, *DTNBP1*, *BLOC1S3*, *PLDN* and *AP3D1* genes is available to confirm the diagnosis.

**Choroideremia:**
The patient's visual field is examined and checked for degeneration of the retina.

Genetic testing is available for some genetic variants that cause choroideremia.

### Ciliopathies

**Primary Ciliary Dyskinesia (PCD):**
PCD is diagnosed through examination of lung or sinus tissue obtained from a biopsy. Screening for levels of nasal nitric oxide is helpful to identify individuals who may have PCD and should proceed for a biopsy.

Clinical genetic testing is available for some of the genes associated with PCD. However, due to biological and phenotypical heterogeneity, different diagnostic tests have to be combined to confirm PCD diagnosis.

**Polycystic Kidney Disease (PKD):**
Diagnosis is established by a thorough clinical evaluation, a complete patient and family history, and imaging techniques, such as ultrasonography, computed tomography and magnetic resonance imaging, for individuals with symptoms consistent with the disease.

Molecular genetic testing is available to confirm the diagnosis.

**Joubert Syndrome:**
Diagnosis is based on physical symptoms and the "molar tooth sign" as seen on an magnetic resonance imaging.

Molecular genetic testing is available. Carrier testing and prenatal diagnosis are available if one of these gene mutations has been identified in an affected family member.

**Asphyxiating thoracic dystrophy (Jeune Syndrome):**
The diagnosis of Jeune Syndrome is based on X-Ray findings. In some cases, the diagnosis may be inferred before birth if characteristic signs and symptoms are present on ultrasound. The diagnosis can be confirmed by genetic testing.

**Bardet-Biedl Syndrome:**
Diagnosis is generally based upon the identification of characteristic findings. Considering that Bardet-Biedl Syndrome is associated with variable expression of the classical features, some patients may not have a clear diagnosis for many years.

Genetic testing may help confirm the diagnosis for some patients.

## TREATMENT HORIZON

### Lysosomal Diseases

**Lysosomal-Storage Disorders (LSDs):**
There is currently no cure for lysosomal-storage disorders, and there are not yet specific treatments for many of these diseases. However, progress is being made regarding

therapies, and there are treatments available for some lysosomal-storage disorders that greatly improve the quality of life of patients.

Furthermore, enzyme replacement therapy has proven effective for individuals with Gaucher disease, Fabry disease, mucopolysaccharidosis (MPS) types I, II, and VI, and Pompe disease (PD). Substrate reduction therapy is an alternative treatment option for patients with Gaucher disease unwilling or unable to receive enzyme replacement therapy.

**Griscelli Syndrome (GS):**
Bone marrow transplantation is the most effective treatment for Griscelli Syndrome type 2.

**Hermansky-Pudlak Syndrome (HPS):**
Treatment of HPS patients with excessive bleeding may consist of transfusions of normal blood platelets. Women with excessive menstrual bleeding can be treated with oral contraceptives. Desmopressin acetate can also be administered to patients with acute bleeding and has proven effective for some patients with this symptom.

Patients with HPS types 1, 2 or 4 who develop pulmonary fibrosis may eventually need a lung transplant.

**Choroideremia:**
The symptoms of choroideremia can be treated but the disease itself cannot yet be cured. This disease is a good candidate for treatment by gene therapy and clinical trials are ongoing.

## Ciliopathies

**Primary Ciliary Dyskinesia (PCD):**
Airway clearance therapy is used to keep the lung tissue healthy for as long as possible. Antibiotics, bronchodilators, steroids and mucus thinners are also used to treat PCD. Routine hearing evaluation is important for young children, and speech therapy and hearing aids my help children with hearing loss and speech problems. Lung transplantation is an option for severe lung disease. Surgery may be indicated if heart defects are present.

**Polycystic Kidney Disease (PKD):**
There is no cure for PKD. However, many supportive treatments can be done to control symptoms, including: control of blood pressure; prompt treatment with antibiotics of a bladder or kidney infection; lots of fluid when blood in the urine is first noted; medication to control pain; healthy lifestyle, including drinking plenty of water and avoid caffeine.

**Joubert Syndrome:**

Developmental delays are usually treated with physical therapy, occupational therapy, speech therapy and infant stimulation. Annual screening is recommended for liver, kidney and retinal abnormalities.

**Asphyxiating thoracic dystrophy (Jeune Syndrome):**
Treatment is based on the symptoms present in each person. In very severe cases, mechanical ventilation may be necessary shortly after birth and surgical interventions may be recommended. In those who are less severely affected, respiratory infections should be aggressively managed to prevent or delay respiratory failure.
Dialysis and renal transplantation may be indicated for people with kidney problems.

**Bardet-Biedl Syndrome:**
Treatment generally focuses on the specific symptoms present in each individual. Progressive vision loss should be accompanied by a specialist, who should provide vision aids and mobility training, if needed. Management of obesity is done with education, diet and exercise and management of intellectual disability, done by special education and speech therapy. Hormone levels should be monitored.

[SEARCH]

[CONTACTS]

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