

**Balneology Research Institute p.r.i.  
Mšené Lázně , Czech republic**



**Remarks on the use of EBM  
( Evidence based medicine )  
in spa research**

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# Introduction

- Balneotherapy - spa treatment with mineral waters (hydrotherapy), gases (radon, carbon dioxide, hydrogen sulphide) and peloids (peat, peat and mud) - in short - natural remedies - is one of the oldest forms of therapy.
- It helps people and improves their quality of life. Otherwise they wouldn't have been searching for it for millennia. But how is actually useful respectively - how does it work?
- This paper deals mainly with osteoarthritis(OA).

# This is not the focus of spa research

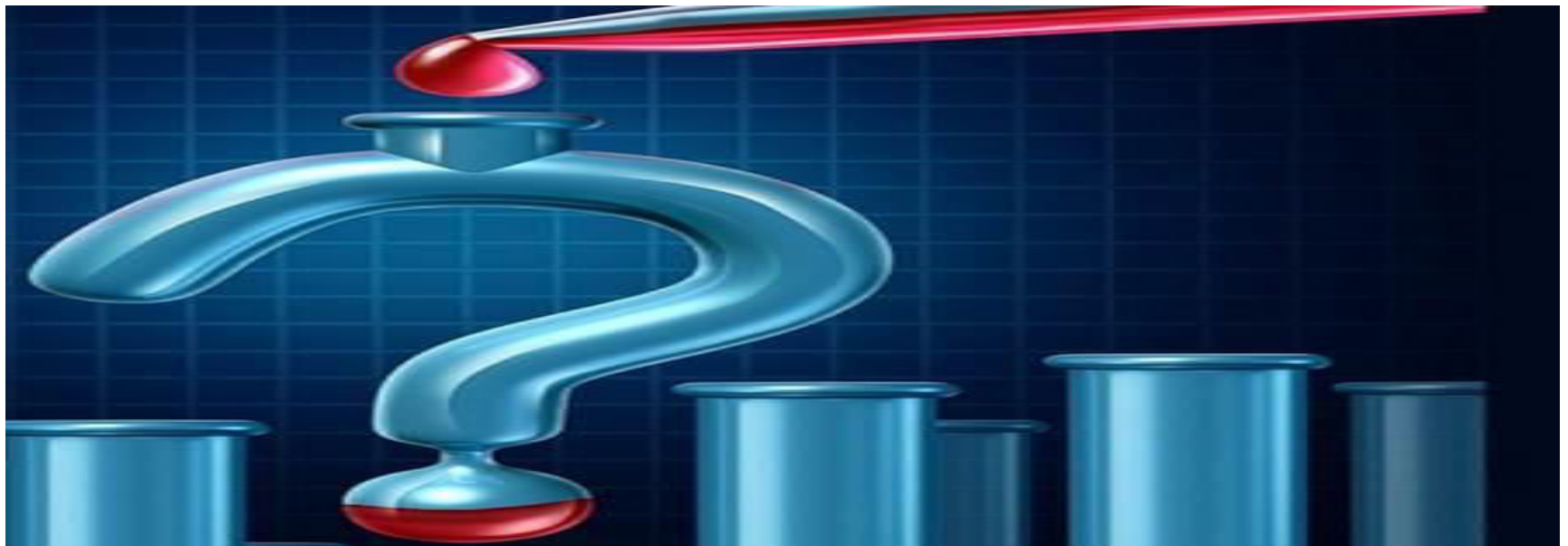
## WELLNESS, VELLBEING



This too  
**WELLNESS, VELLBEING**



# Our interest is in EBM used in spa research by **BIOMARKERS & IMMUNOMARKERS & OTHERS**



# The level of many studies in spa research is poor

- By systematically reviewing many studies around the world, it can be concluded that the positive findings in the treatment of various types of diseases contained in most of these studies cannot be ignored. However, the scientific evidence presented by these studies is weak due to **poor methodological quality**. Further research should avoid errors in reviewed studies (randomized and non-randomized) included numerous errors described in meta-analyzes, identified by **methodological inconsistency, multi-factorial effects, use various natural remedies, non-uniforms, not comparable, and non-reproducibility**.

# What other mistakes are in this works?

- To rely on the results obtained by **subjective evaluation by patients** and with **subjective opinions physicians** using **questionnaires**.
- In many studies it is **WOMAC** – (Visual Analog Scale for Pain Assessment) to assessment of OA for pain, stiffness and joint function: especially the knee, hip, spine, shoulder and hands.
- Another frequent questionnaire is **SF-36** (Short Form 36) to assessment of wellbeing.
- **Other** were also used.
- **It is essential that this is a subjective evaluation.**

# Subjective approach



Research based on these questionnaires and observations is good for marketing purposes and asking other questions suitable for continuing with deeper research.

**This subjective approach is  
of low scientific value.**



# Effect natural remedies & EBM

- This is a relevant but controversial topic that requires an **in-depth systematic review** in the style of Cochran's reviews. We miss this in spa research. In the first place, serious and high-quality studies are lacking to confirm and bring to deeper understanding of the effects of natural remedies used in balneotherapy.
- The lack of objective evidence emphasizes the **importance of detecting the processes arising in spa treatments** by using natural remedies.

# Processes

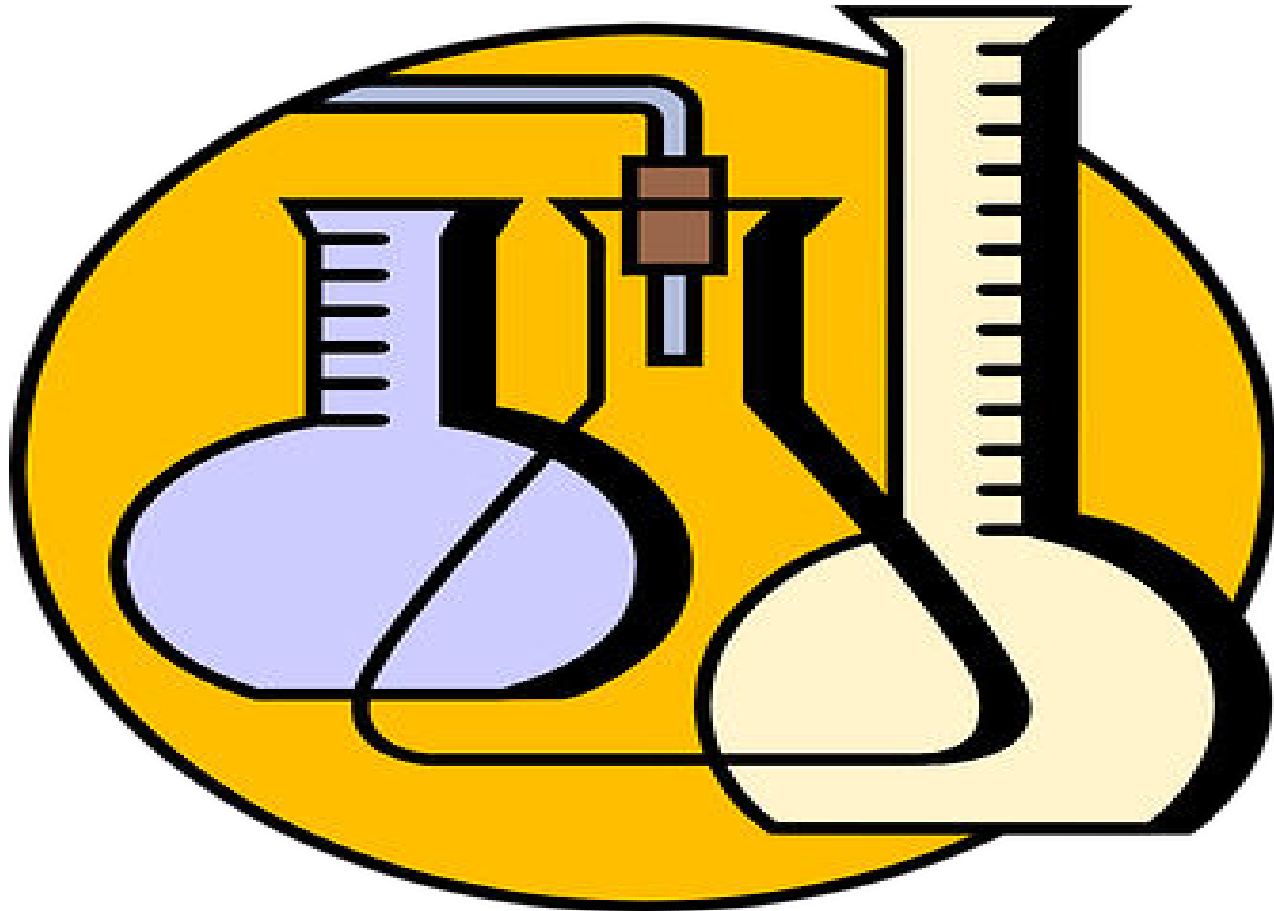
- **It must be with a reflection on :**
- biochemical processes,
- hormonal processes,
- immune system processes,
- the detection of signaling pathways,
- molecular biological processes,
- epigenetic and genetic processes.
- **All processes leading to a positive effect in spa treatment.**

# EBM

And this approach is Evidence Based Medicine(EBM) in spa research of balneotherapy. Respectively objectively established and assessed evidence.

**This approaches EBM are recognized by clinicians.**

**Determination of markers by scientific methods:  
biochemistry analysis, imunochemistry analysis,  
liquid biopsy, Mass spectrometry, Next Generation  
Sequencing & so on.**



# Parameters

- **Within EBM it is necessary to select objectively observable parameters:**
- biomarkers, neurotransmitters, enzymes, hormones, receptors, receptor inhibitors, factors involved in specific tissue metabolism, genetic-level regulatory molecules, immunomarkers, acute inflammatory phase proteins, individual cellular components of the immune system and blood, cytokines, interleukins, tumor necrosis factor, specific suppressors and stimulatory factors, growth factors and their inhibitors etc.

# Micro RNA & biomarkers

- Research directed towards EBM can objectively demonstrate, for example, the epigenetic effect of mineralized waters recognized as a therapeutic agent or of peloid components used in spa treatment of osteoarthritis. It is possible, for example, to **measure selected micro RNAs and their regulated protein biomarkers** that are involved in osteogenesis and chondrogenesis. Immunomarkers with signaling pathways can be evaluated too.

# Hypothesis of epigenetic effect

- The well-known effect of **time-limited positive effects of spa therapy** with hydrotherapy and peloids on osteoarthritis lasting for about **6 months** would be consistent with the **hypothesis** that when peloids are applied in osteoarthritis, there is a direct **epigenetic effect on genes responsible for protein production**. However, this effect is reversible over time and may correspond to re-enabling transcription of switched genes.
- **Turning off genes** responsible for protein expression for **catabolic functions** (eg, cartilage or bone resorption) or
- **turning on genes** for protein expression for **anabolic functions** (cartilage production) in chondrogenesis
- can play a **crucial role** in the progression of osteoarthritis. This hypothesis can be confirmed or refuted by quantitative determination of selected microRNAs and their regulated protein biomarkers.

# Problems in Czech Republic

- Technical skills and equipment to carry out such research as well as staffing is available. However, there is currently insufficient funding for studies of this type to support molecular-biological research.
- In view of this, it is difficult, at least in the Czech Republic, to promote research in spa treatment of this character, corresponding to evidence-based medicine.
- Doing so but this are objective evidences with a comprehensive approach in the statistical and multidisciplinary evaluation of selected markers.



# Problems in Czech Republic

- It is known that most of the discoveries were made at the interfaces of disciplines. In the case of spa treatment, this is problematic because balneology as a field does not exist in the Czech Republic and is included in the field of **Rehabilitation and Physical Medicine - RFM**. Therefore, it is difficult to promote research in this area.
- Yet we do not lose hope and do everything we can to accomplish targeted research in balneology. Even through repeated applications in grant agencies. However, the evaluation of the project in its assessment for the purpose of awarding the grant according to the set criteria of the challenger remains a problematic.

# Problems in Czech Republic

- To illustrate, one of the possible evaluation criteria is the **continuity of research** in this area. In the Czech Republic, the original Balneology Research Institute State Enterprise was abolished after the Velvet Revolution in 1991 without compensation. The newly established Balneology Research Institute public research institution was established in 2011. No balneological research has been carried out in the Czech Republic from 1991 to 2011. Thus, the criterion of continuity of research and the guarantee of project implementation by researchers with appropriate **publication activity** and a sufficient Hirsch index relative to publications in recognized journals could not be met.

# Problems in Czech Republic

- This handicap led to the fact that even a well-prepared project was not awarded a grant, in some cases even with a minimum point difference to the limit for achieving it. Although the problem described does not fall within EBM in spa research, this problem makes it impossible to implement quality projects based on EBM foundations.

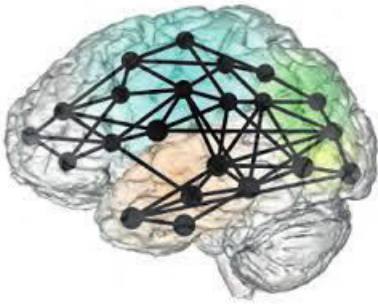
# European fund for the promotion of research in balneology

- The described situation in the availability of resources for research in balneology could be improved if the **strategy for research** in balneology within the EU will be **changed**.
- **Should be based a European fund for the promotion of research in balneology with the support of the European Spas Association**.
- Such a spa research fund could assess the allocation of funds to **quality projects competing** in the competitive struggle with established criteria for a specific area of spa research and its application in balneotherapy.

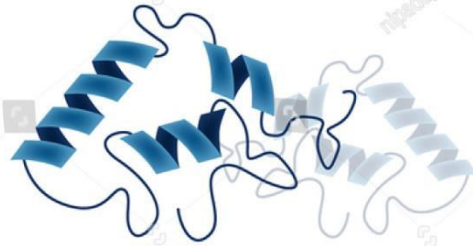
We will stay only at this level?



# PROTEINS BIOMARKERS



## PROTEIN infographic



## Function



### Enzyme

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consectetur adipiscing  
sed do eiusmod tempor  
Sucrose, Trypsin



### Structure

Lorem ipsum dolor sit  
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sed do eiusmod tempor  
Collagen, Keratin



### Transportation

Lorem ipsum dolor sit  
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Hemoglobin



### Antibody

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Immunoglobulin



### Hormone

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Insulin,  
Growth hormone

## SOURCES of PROTEIN



## 40-50 g Daily



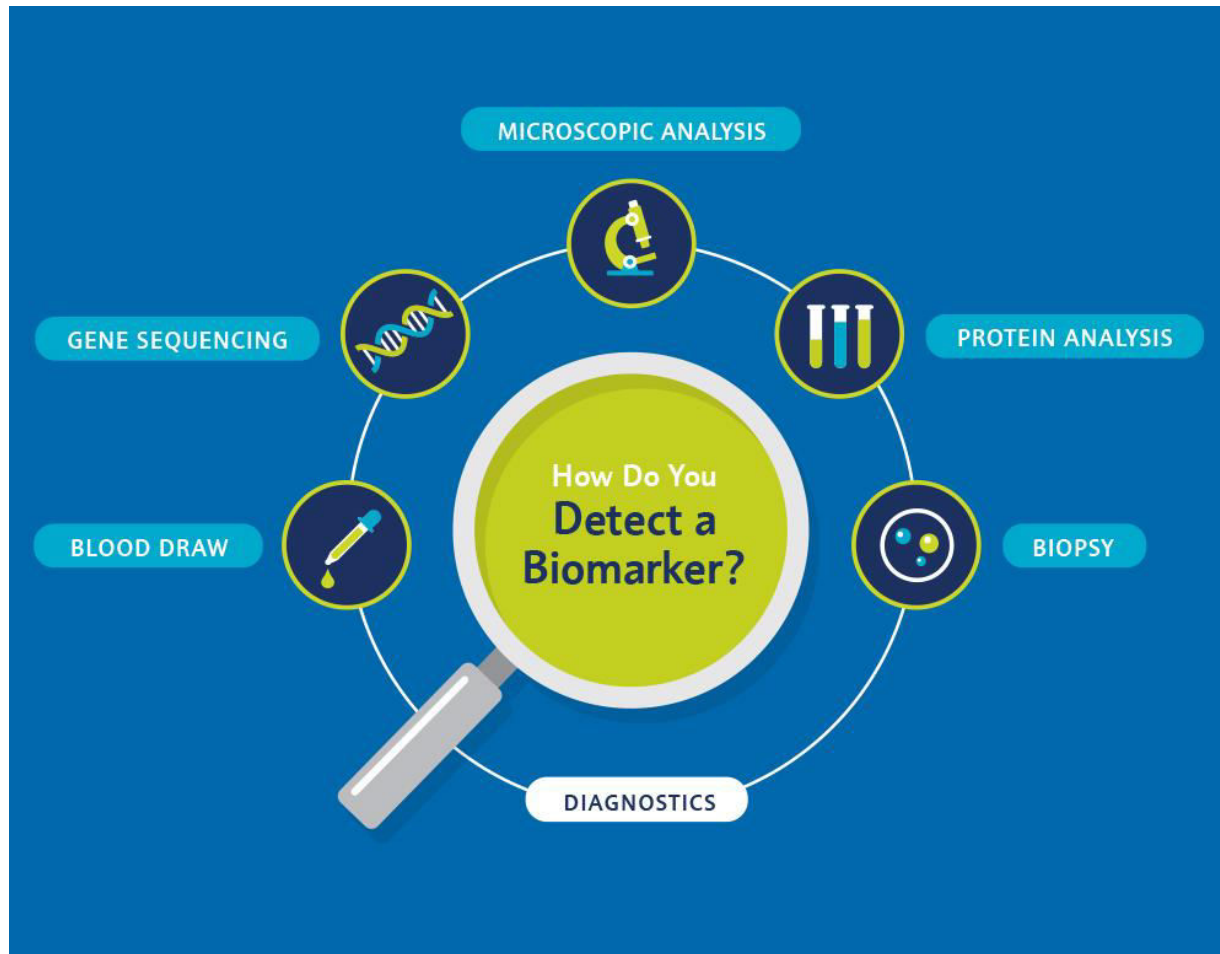
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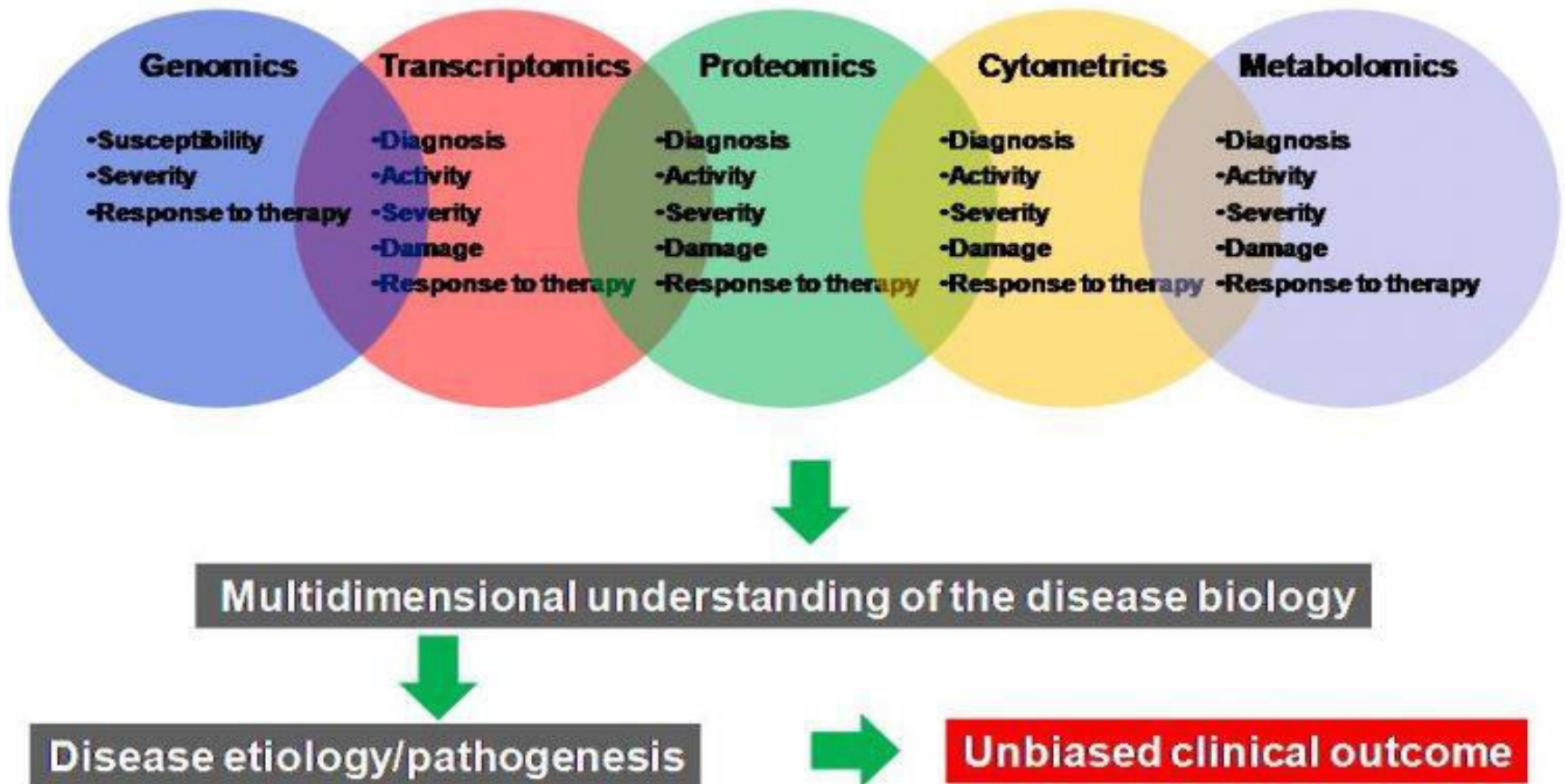
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# DETECTION OF BIOMARKERS

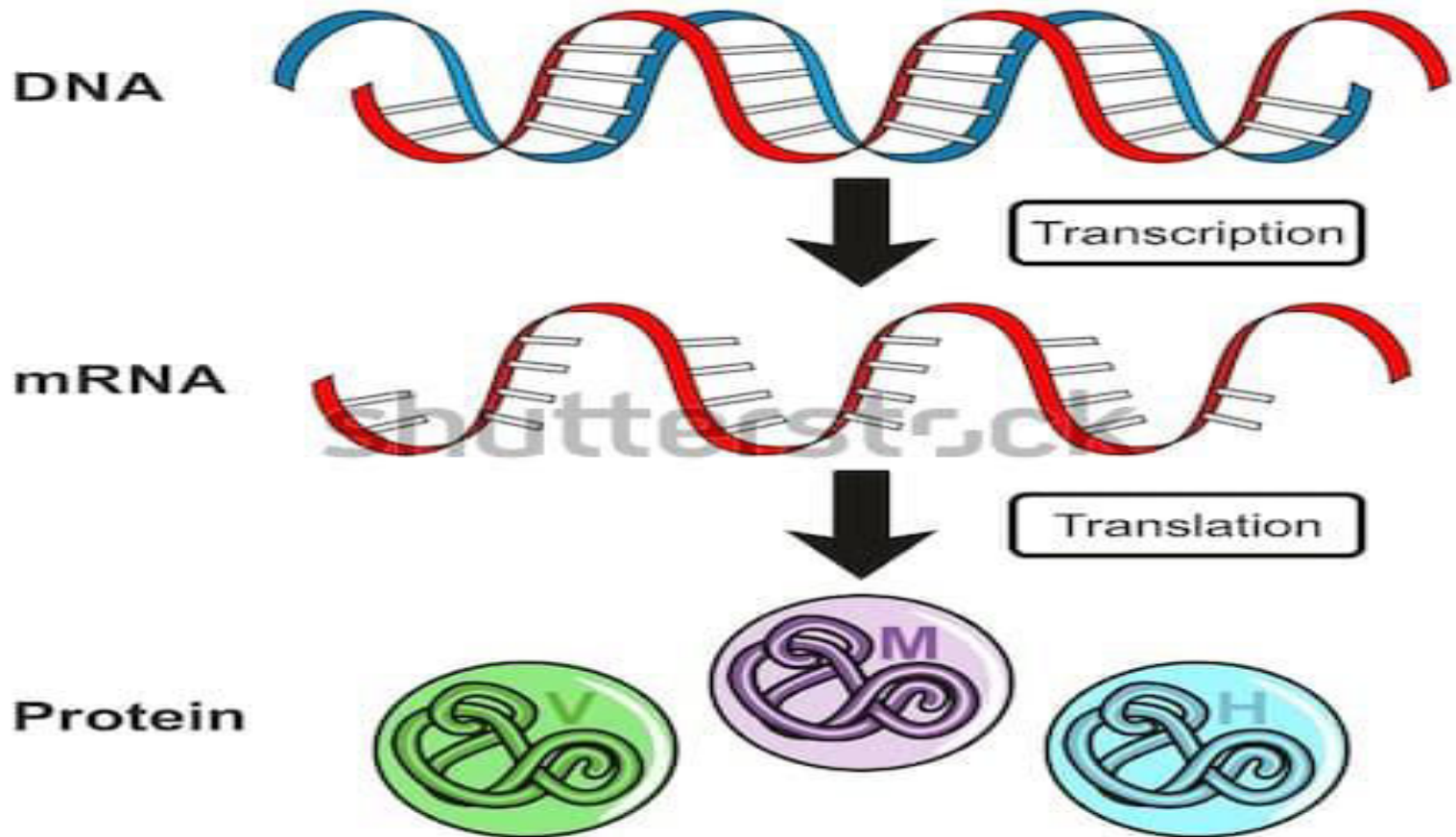


# Multidisciplinary research

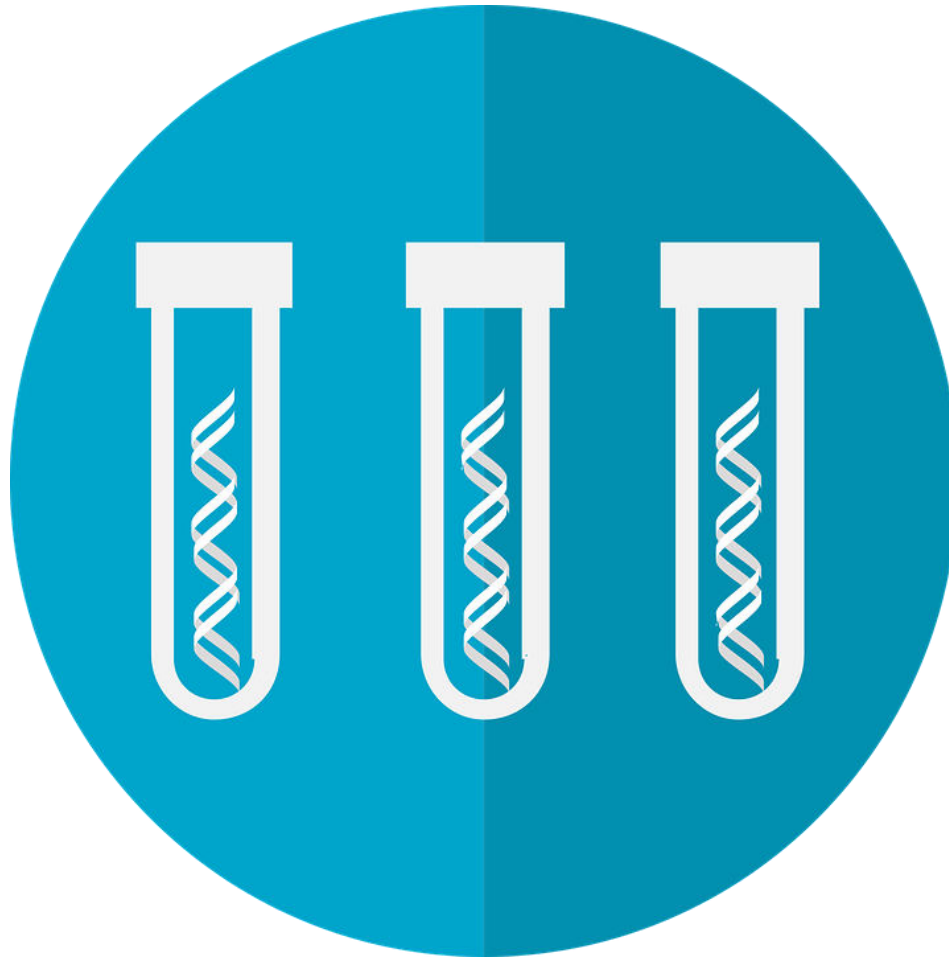




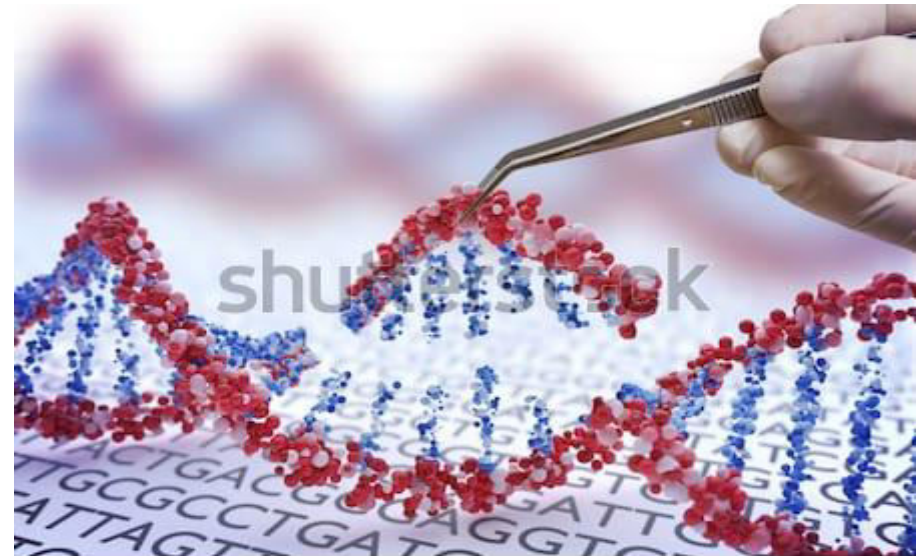
# Genesis of proteins



# NGS-NEXT GENERATION SEQUENCING



# Modern laboratory methods for determination of biomarkers and epigenetic effects of environmental influences



Medicine is already deepening the knowledge of molecular, proteomic, metabolomic, genetic and epigenetic level



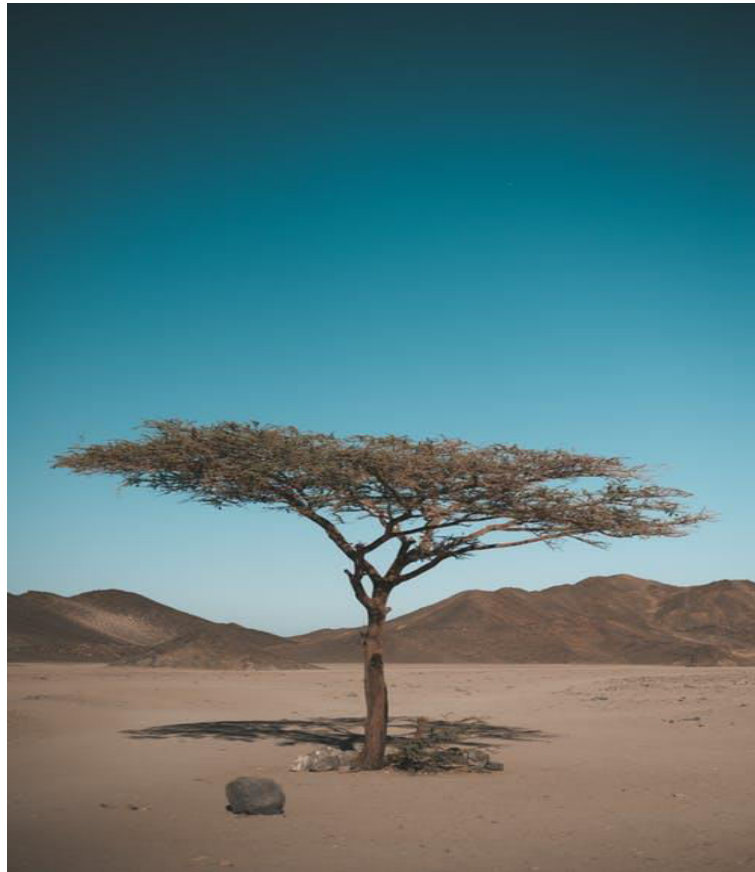
Balneology research institute p.r.i.  
Mšené Lázně, Czech Republic,  
offers cooperation in spa research



# International cooperation



The dry tree of knowledge without water is  
the same as science and research without  
money !!!



**Thank you for attention**

