EPI | RE | C EPILEPSY RESEARCH CENTRE PRAGUE

Epilepsy Research Centre Prague

VISION

- Outstanding epilepsy research – paving the way to a life seizure free

MISSION

- We aim to transform the lives of people with epilepsy through high-quality research, rapidly translated into patient benefit.

WHY THIS CENTRE?

- The current existence of multidisciplinary teams of senior and junior scientists who are passionate about and committed to epilepsy research
- The presence of a solid infrastructure for fast bench-to-bedside translation of experimental discoveries and innovations to clinical practice
- The introduction of state-of-the-art research tools into epilepsy research to bring breakthroughs into the understanding of epilepsy and seizures
- The exponential growth in disruptive technologies in medicine has the potential to transform epilepsy treatment and replace existing therapeutic approaches

WHAT DO WE WANT TO ACHIEVE

- To understand the causes and mechanisms of epilepsy and seizures.
- To find a cure for epilepsy and improve the quality of life for people with epilepsy and their families.
- To create an internationally recognised centre, pioneering future epilepsy research.
- To build a team of teams with the capacity to tackle the most challenging aspects of epilepsy.
- To set up a centre with an efficient organization and management structure that will support high-profile epilepsy research.
- To create an environment of excellence that will attract young scientists and clinicians with a passion for epilepsy.

CHALLENGES

- The absence of effective management and a clearly defined research purpose
- The existence of multiple teams from various institutions (legal bodies)
- The lack of efficient internal communication and medium- to long-term strategic planning
- The absence of clear organisation and a focused direction for epilepsy research
- Insufficient numbers of young scientists and the absence of a career development programme for young scientists
- Unstable financing of the research

HOW TO ACHIEVE THESE GOALS

- **Build a team of teams with a well-defined research strategy, organization and clear research focus**
  - A steering committee and project management to determine and oversee/coordinate the research strategy
  - Organization into multiple teams with expertise in various research techniques
- **Strong interdependence within the research environment and close collaboration between multi-disciplinary research groups**
  - Communication across the teams via shared progress meetings, formal bulletins, etc.
  - Joint project preparations
- **Disciplined action focused on the fundamental aspects of the research strategy**
  - Research focused on various aspects of malformation due to abnormal cortical development (MCD), with particular focus on focal cortical dysplasia
  - Ictogenesis and epileptogenesis in MCD
  - Neuroimaging and clinical neurophysiology in MCD.
  - Molecular neurobiology of MCD.
- **Build a culture of freedom and responsibility, but within a defined framework of the research strategy**
  - Each member has a well-defined purpose and goal to accomplish and is aware of their role within the strategy.
  - Promote discipline and responsibility within the teams, and simultaneously allow autonomy and the freedom in the realization specific tasks.
  - Establish an influential culture, focused on excellence in epilepsy research.
  - Recruitment of suitable people with a shared purpose and passion for the vision and mission of the centre.
  - Collaboration with external stakeholders, including patients' organizations.
- **The utilisation of technological advances as research accelerators**
  - Genetic manipulation (optogenetics, chemogenetics, etc)
  - State-of-the-art *in vivo* imaging and electrophysiological techniques
  - Neuroimaging in humans
  - Cell cultures and molecular neurobiology
  - Gene therapy
- **Well elaborated career-development programme for early-career scientists with a focus on interdisciplinary and translational research**
  - Regular and early-in-career exposure of scientists to the clinical environment and clinicians to the scientific environment.
  - Secure job positions and funding for resources and staff for early-career scientists
  - Mentoring programme, Leadership and other forms of training

1. PROBLEM SUMMARY

Epilepsy is a common brain disorder affecting one person in every hundred. Seizures in every third person with epilepsy cannot be controlled with drugs. Pharmacoresistant epilepsy is one of the leading causes of long-term disability, results in a poor quality of life for patients and their families and represents a substantial economic and social burden.

Epilepsy has been intensely studied for decades, but we still do not understand its mechanisms. New drugs are continually introduced into clinical practice, but their impact is minimal and the proportion of patients with severe pharmacoresistant epilepsy remains unchanged. New and effective therapies for epilepsy are urgently needed. To find a cure for epilepsy and to restore the quality of life for people with epilepsy requires a major paradigm shift away from traditional approaches to epilepsy research and drug discovery.

Currently, we are living in an era of a technological revolution. Medical knowledge, medical procedures and treatment protocols, pharmacological advances and medical technology all are advancing at unprecedented speeds. New technologies being developed have the potential to transform future healthcare. In epilepsy, the implementation of disruptive research technologies like gene therapy, molecular pharmacology and artificial intelligence, could significantly change disease outcomes by improving diagnosis, identifying new causes and discovering novel treatments. Therefore, scientists, medical professionals and administrators must learn to be open-minded and flexible, and to aspire to new visions and far-reaching goals.

To address these issues, we aim to create a multidisciplinary epilepsy research centre with the ambition to make major breakthroughs in the mechanisms of the most severe and intractable epilepsies in adults and children. The centre's ultimate goal is to pave the way for the development of new strategies to cure epilepsy.

2. SOLUTION SUMMARY

EpiReC is a "team of teams" type of organisation composed of small teams of experts from multiple research disciplines. The centre structure is characterized by the strong interdependence of the operating environment, the tight interconnection between the teams and disciplined practice by team members. The joint purpose and passion, clearly defined research mission and multidisciplinary nature of the centre guarantees an effective approach to study the principles of epilepsy, to develop new treatments and to rapidly translate the discoveries from laboratory-to-patient (bench to bedside?).

The centre is created on the solid foundations of already existing collaborations between neurologists, neuroscientists, molecular biologists, engineers, mathematicians, and physicists, who share a common interest in epilepsy research. The team of teams will have the capacity to tackle the most challenging aspects of epilepsy research by effectively combining expertise from various disciplines and by a well-determined organisational structure and strategic planning. The most important and unique aspect of the centre's personnel composition and philosophy is that the centre team is assembled from people with similar interests, work ethic and a common goal.

The centre has the ambition to become a leading epilepsy research organisation that will determine the future direction of research and develop future epilepsy treatments, especially in the field of intractable epilepsies caused by malformations of cortical developments. The implementation of new molecular diagnostic techniques and

gene therapy targeting crucial disease mechanisms are steps towards effective and personalised (precision) epilepsy therapy.

3. EXECUTION AND NEXT STEPS

3.1 Structure

The centre is established by a group of senior clinicians and scientists who are internationally recognised experts in the field of epileptology or epilepsy research. The proposed organization is based on the foundation of an existing collaboration between several members of the centre. The Steering Committee defines and approves the strategy of the centre while the Management is responsible for managing the project activities. The Scientific Advisory Board is composed of internationally recognised experts in various fields of epilepsy research and clinical epileptology, a member of the pharmaceutical company (Prof Deuderwaerdere) and founder of the internationally recognised research centre Childhood Leukaemia Investigation Prague (Prof Stary). To tackle the research objectives, the centre will be organized into research groups specialized in various research techniques and methodological approaches. Each group provides specific expertise to the joint projects, and its leader is responsible for specific aspects of the research strategy. This approach should guarantee a complex approach to the research goals and fast translation of experimental observation into clinical practice and *vice versa*.

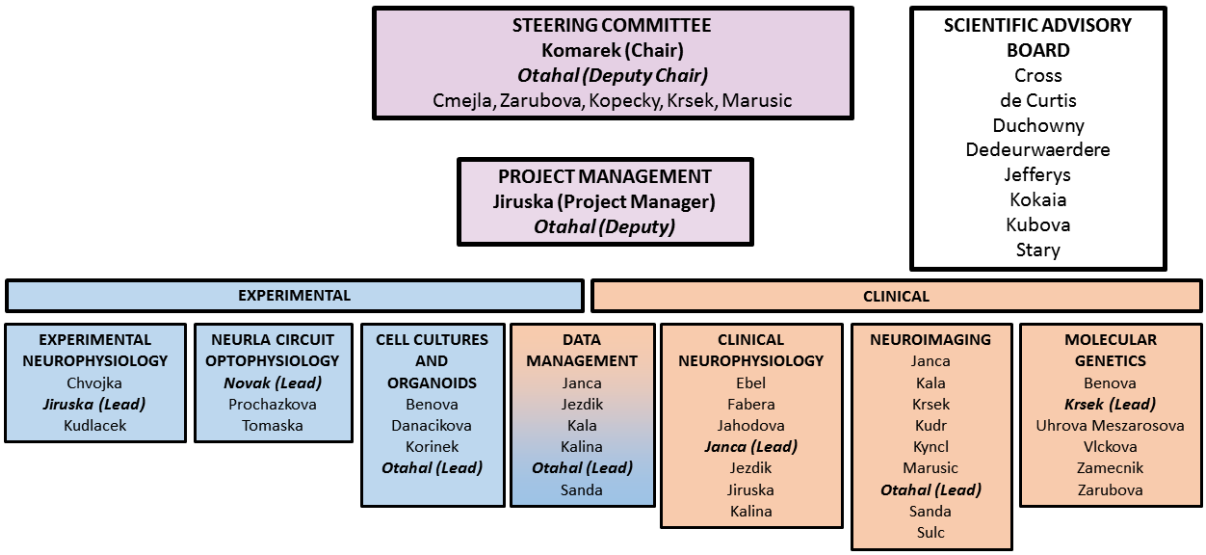

Figure 1. The organization of EpiReC

3.2. Research goals

The existing members and groups of the EpiReC are recognized for their research focused on the mechanisms of epileptogenesis and ictogenesis, organization of epileptic networks, neuroimaging, epilepsy surgery, malformations of cortical development and molecular genetics of epilepsy. The pilot research initiative of the centre will focus on the complex approach to our understanding of the most common cause of pharmacoresistant epilepsy – focal cortical dysplasia (FCD). The specific goals are:

- The elucidation of the cellular and network mechanisms that govern epileptogenesis and seizure genesis in humans and animals with focal cortical dysplasia.
- Identification of biomarkers that will delineate epileptogenic tissue in FCD-related epilepsy to improve presurgical diagnosis and outcome of epilepsy surgery.
- Understanding the molecular and genetic mechanisms involved in FCD and other malformations of cortical developments.
- The innovation of existing diagnostic and therapeutic approaches to FCD-related epilepsy and evaluation of gene therapy to control seizure genesis and disease progression in FCD.

Research focused on FCD will be the centre's research niche. Fortunately, we have a critical mass of researchers with relevant expertise and passionate about this topic, who could establish EpiReC as the global leader in FCD research.

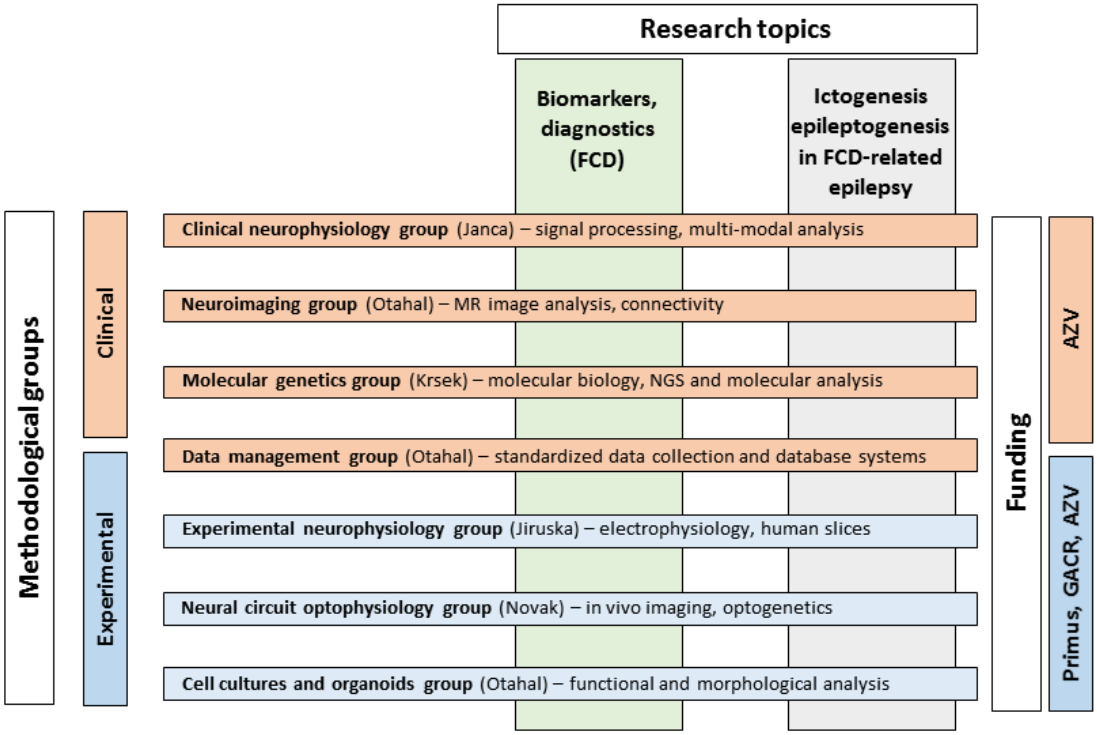

Figure 2. The role of individual groups within the research theme oriented on FCD-related epilepsy

4. COMPETITION

The multidisciplinary organisation of the EpiReC, the vertical nature of its research strategy, ranging from molecule to brain and the focus on rapid translation will create an organization that will be highly competitive to world-leading epilepsy and brain research centres. However, the moderate size of the centre and the integrated management strategy will guarantee focused research and close interactions between teams.. The advantage of our centre is also expressed by the availability of both experimental and clinical approaches to epilepsy research which will have rather synergistic than additive effect.