Comprehensive Exam Question: Translational

Epilepsy is one of the most common disorders of the nervous system. There are many types of epilepsy, but they all are characterized by recurrent, unprovoked seizures and associated behavioral changes. In epilepsy, the normal electrical events in the brain become disrupted. Unfortunately, the cause of epilepsy in the majority of cases is unknown, making it challenging to find a suitable treatment. Over the years, however, basic research using animal models of epilepsy and seizures has significantly advanced our understanding of the biological mechanisms and possible therapeutic targets of epilepsy. More recently, the discovery of specific genes underlying certain epilepsies has also added to our knowledge of the diversity of epilepsy pathogenesis. As our understanding of the etiologies of epilepsy and physiology of seizures increase, new treatment methods based on cutting-edge technologies are becoming a real possibility.

For this comprehensive exam question, you will need to:

1. Provide a general overview of seizures and epilepsy, including classification of seizure types and current treatment options.

2. Describe the current understanding of the neurobiological basis for epileptic seizures at the cellular, synaptic, and circuit level. Include the related physiological events to seizure type and pattern of spread.

3. Based on animal models, compare and contrast at least two genetic mutations associated with epilepsy, specifically detailing how these abnormal gene products can disrupt normal neuronal and circuit function.

4. Integrate your responses above to generate a plausible hypothesis about a potential therapeutic approach utilizing a new molecular technique that can manipulate gene expression or neuronal activity (e.g., RNA Interference, antisense technology, CRISPR, optogenetics, or chemogenetics). Justify the choice of technique, describe concisely the goals of your proposed research and summarize the expected outcome(s), including the impact of the proposed research that will have on the field.

The four parts of this comprehensive exam will be weighted equally to determine your overall grade. Answers should be between 10 and 15 typed double-spaced total pages in length, excluding references.