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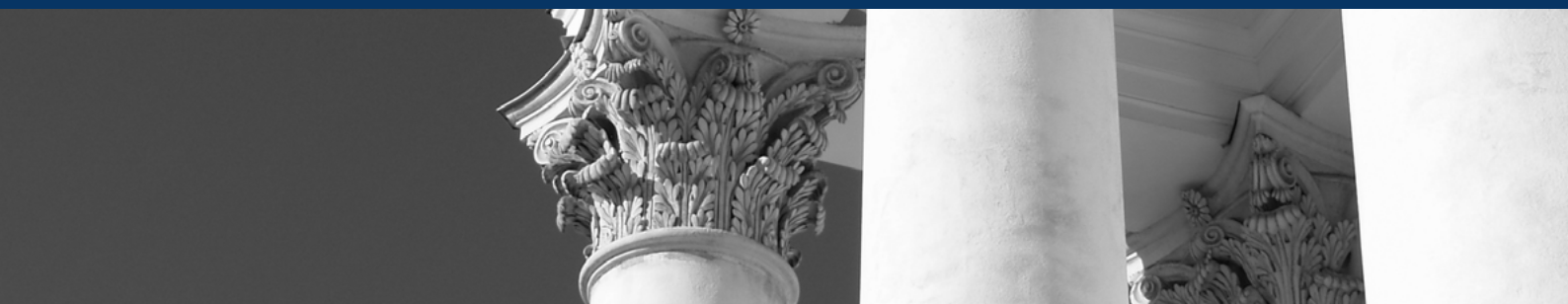
"IULIU HATIEGANU" UNIVERSITY OF MEDICINE AND PHARMACY DOCTORAL SCHOOL

NEUROSCIENCE

PROGRAM

2016-2017 | SECTION 6

28 MARCH | UMF "IULIU HATIEGANU" | CLUJ-NAPOCA | ROMANIA



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CEO of Neuropore Therapies Inc., San Diego, USA

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2016-2017

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COURSE PROGRAM

COURSE PROGRAM

MARCH 28TH, 2017

"MULTIMEDIA" AUDITORIUM, "IULIU HATIEGANU" UMF CLUJ-NAPOCA

8 VICTOR BABES STREET | CLUJ-NAPOCA | ROMANIA

09:50 – 10:00	Dafin F. Mureșanu /Romania Welcome address
10:00 – 10:45	Peter Jenner /UK Parkinson's disease in the modern era: A single disease or a syndrome
10:45 – 11:30	Peter Jenner /UK Drug treatment of Parkinson's disease: dopaminergic therapies and the avoidance of motor complications
11:30 – 12:00	Session Break
12:00 – 12:45	Peter Jenner /UK Non-motor and non-dopaminergic approaches to treating Parkinson's disease
12:45 – 13:30	Peter Jenner /UK Pathogenic mechanisms and neuroprotection/neurorestoration in Parkinson's disease
13:30 – 14:30	Session Break

MARCH 28TH, 2017

"MULTIMEDIA" AUDITORIUM, "IULIU HATIEGANU" UMF CLUJ-NAPOCA

8 VICTOR BABES STREET | CLUJ-NAPOCA | ROMANIA

14:30 – 15:15	Peter Jenner /UK Small group discussion of future approaches to Parkinson's disease and student presentations
15:15 – 16:00	Dieter H. Meier /USA Parkinson's disease - diagnosis, classification and treatment of early disease
16:00 – 16:30	Session Break
16:30 – 17:15	Dieter H. Meier /USA Parkinson's disease - treatment of advanced disease
17:15 – 18:00	Dieter H. Meier /USA Parkinson's disease - treatment development for the future

INTERNATIONAL GUEST LECTURERS

PETER JENNER
UK

Prof Peter Jenner Peter is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He has expertise in drug metabolism and pharmacokinetics but neuropharmacology based on functional models of neurodegenerative diseases has formed the major focus of his work. Following 14 years as Head of Pharmacology, Peter is now Emeritus Professor of Pharmacology at King's College London, and a Fellow of the Royal Pharmaceutical Society, the British Pharmacological Society, the Royal Society of Medicine and of King's College London He has published more than 700 peer reviewed papers along with many chapters and monographs. Aside from his illustrious academic achievements, Professor Jenner also has considerable industrial experience, being a Founder, Director and CSO of Proximagen, is currently CSO of Chronos Therapeutics and consults for a number of pharmaceutical companies, including USB, Teva and Lundbeck.

Professor Peter Jenner Currently Emeritus Professor of Pharmacology at King's College London, Peter is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He was previously a founder and CSO of the biotech Proximagen and is also currently CSO of Chronos

DIETER H. MEIER

USA

As a board certified neurologist, Dieter H. Meier was engaged over the last 20 years in a number of industry positions, mostly in drug development and general management. His contributions to the drug development at various stages let to the registration of e.g. Actilyse for stroke, Pramipexol and Apomorphine in Parkinson's Disease (PD), and the development of several earlier approaches.

Most recently, his team of scientists developed several small molecules interacting with α-Synuclein. One of these molecules was partnered with a large pharmaceutical company, and is jointly being developed in the clinic with the target to modify the course of PD.

Dieter H. Meier advises international companies on clinical and strategic developments. He serves on university and industry Advisory Boards; eg. for Neuropore Therapies Inc., a San Diego based company, dedicated to the research and development of drugs interacting with misfolded proteins aiming at changing the course of neurodegenerative diseases.

ABSTRACTS

PARKINSON'S DISEASE IN THE MODERN ERA: A SINGLE DISEASE OR A SYNDROME

PETER JENNER
King's College London, UK

Parkinson's disease (PD) is classically considered as a disorder of movement characterised by nigral dopaminergic cell degeneration, striatal dopamine loss, a good response to L-dopa and the presence of Lewy bodies in remaining neurones. However, a newer view of PD is emerging as a multisystem, multi-organ disorder involving numerous neurotransmitter systems that progresses through the brain. The result of this sweeping pathology is that PD is a multi-symptom illness where non-motor components are of greater importance than the motor features and where dopaminergic neuronal loss is only a minor component of the pathology. However, there is no fixed pattern to the pathology of PD and the progression of neuronal loss can result in different patterns of symptom appearance that lead to the idea that there are subtypes of PD and that it is a syndrome rather than a single illness.

DRUG TREATMENT OF PARKINSON'S DISEASE: DOPAMINERGIC THERAPIES AND THE AVOIDANCE OF MOTOR COMPLICATIONS

PETER JENNER
King's College London, UK

The drug treatment of Parkinson's disease (PD) remains centred on the use of L-dopa and dopamine agonist drugs as forms of dopamine replacement therapy. The use of L-dopa is supported by the use of three classes of enzyme inhibitors - dopa decarboxylase inhibitors, COMT inhibitors and MAO-B inhibitors. Both dopamine agonists and L-dopa are available in a range of delivery forms and there is a move to make medications once daily or to provide continuous drug delivery through formulation and route of administration. There is debate about whether dopamine agonists or L-dopa should be used to initiate treatment with currently a return to the early use of low dose L-dopa treatment. L-dopa's use is associated with a high incidence of motor complications and motor fluctuations and these appear associated with both the extent of disease progression and the pulsatile nature of L-dopa's action leading to disruption of basal ganglia function. As a consequence, continuous drug delivery providing a more physiological stimulation of striatal dopamine receptors is being advocated.

NON-MOTOR AND NON-DOPAMINERGIC APPROACHES TO TREATING PARKINSON'S DISEASE

PETER JENNER
King's College London, UK

The pathology of Parkinson's disease (PD) is widespread in brain and affects multiple neurotransmitter systems involved in the expression of both motor and non-motor symptoms of. In the basal ganglia, the loss of dopaminergic input causes alterations in the function of those pathways making up the strio-thalamo-cortical loops that control voluntary movement – and many of these utilize transmitters other than dopamine. As a consequence, there are multiple opportunities to use non-dopaminergic approaches to the treatment of PD to alter symptom expression. However, despite encouraging results in animal models of PD, there has been relatively little translation to man. Some of this may reflect the nature of animal models of PD, other parts may be the side-effect profile seen in man and some may reflect clinical trial design. Interesting examples relate to

the attempts to develop drugs altering serotoninergic function, glutamate antagonists, adenosine antagonists and anticholinergic compounds. The situation with respect to non-motor symptoms of PD is more basic. There is a need to understand the pathological basis of non-motor symptoms and to model these in animals so that pharmacological manipulation can be attempted. Currently non-motor symptoms represent the biggest clinical challenge but are under researched and under exploited.

PATHOGENIC MECHANISMS AND NEUROPROTECTION/ NEURORESTORATION IN PARKINSON'S DISEASE

PETER JENNER
King's College London, UK

The current drug treatment of Parkinson's disease (PD) provides symptomatic relief but it is not aimed at preventing, slowing or reversing the degenerative process. There have been attempts to introduce dopaminergic therapies early in PD to act as disease modifying agents but these have largely failed. Reinstating dopamine production in the basal ganglia is being attempted by using viral vectors containing the genes for key enzymes in dopamine synthesis and stem cell based approaches. Trophic factors that stimulate growth of dopaminergic neurones, for example GDNF and neurturin are still being investigated but there has been a lack of a consistent response in clinical trial. Understanding the pathogenic processes that underlie PD has been reasonably successful by using toxin based animal models, post mortem studies of brain tissue from PD and by understanding genetic causes of the illness. From these investigations, a number of approaches to neuroprotection and neurorestoration have been devised with differing degrees of success. Treatments developed through toxin animal models or through underlying biochemical mechanisms detected in post-mortem brain tissue, have so far, apparently failed in clinical trial. Current studies centre on interfering with processes relevant to molecular changes associated with genetic forms of PD – α-synuclein, LRRK2, GBA, parkin – but (with the exception of α-synuclein) these affect only a small proportion of the patient population. Since α-synuclein toxicity appears relevant to most forms of PD, there is significant interest in antibody, vaccination and clearance based approaches. Lastly, there a lot of activity in repurposing drugs already in use in man for other indications that may be neuroprotective in PD – for example glitazones and calcium antagonists. It is very likely that PD is a syndrome so any specific neuroprotective treatment might only be effective in one patient subgroup.

SMALL GROUP DISCUSSION OF FUTURE APPROACHES TO PARKINSON'S DISEASE AND STUDENT PRESENTATIONS

PETER JENNER
King's College London, UK

After a brief introduction to the task, the participants will be divided in to small groups and asked to discuss a specific question for 30 minutes and to come up with a 5 minute presentation to the whole group.
The question to be addressed is as follows:
'If you were given a laboratory and unlimited funds, what approach would you take to making the next breakthrough in the treatment of Parkinson's disease?'
The issues to be addressed must include feasibility, time to success and the outcome for the patient population.

PARKINSON'S DISEASE - DIAGNOSIS, CLASSIFICATION AND TREATMENT OF EARLY DISEASE

DIETER H. MEIER
CEO of Neuropore Therapies Inc., San Diego, USA

The diagnosis of typical Parkinson's Disease appears to be straight forward if classical symptoms are present. However, particularly early in the course of the disease, the patient may present with 'incomplete' symptoms, or non-classical symptoms, or any combination thereof and still be probably to be diagnosed as PD.
Alternatively, a number of Syndroms may present with parkinsonism. The diagnosis and clinical differential diagnosis of Parkinson's Disease may have ramifications for further treatment.
Once correctly diagnosed, the symptomatic treatment of early Parkinson's disease appears to be relatively straight forward through the substitution therapy of dopamine. However, there are still differing opinions on the utility of L-DOPA and Dopamine-Agonists after several decades since their introduction.
The objective of this lecture is to enable the participant to:

- Correctly diagnose Early Parkinson's Disease vs. other Parkinsonisms
- Initiate early treatments with respect to current well- being and long-term outcome.

PARKINSON'S DISEASE - TREATMENT OF ADVANCED DISEASE

DIETER H. MEIER
CEO of Neuropore Therapies Inc., San Diego, USA

With progressing disease, possibly as a result of previous therapies, symptoms of later stages of PD become increasingly difficult to treat. It has been proposed that long-standing treatment may lead to "L-Dopa induced" (motor) fluctuations.
Initially oral therapies are being recommended and part of treatment guidelines. Several therapies have been proposed not only alleviate the symptoms of PD but (also) to slow or halt the course of the disease progression. At a subsequent stage patients may not be adequately controlled through oral or noninvasive therapies. At this stage, depending on the clinical pathology, the general conditions of the patient and the availability of the treatments a few treatment options are available which include two main avenues, deep brain stimulation (DBS) or continuous application of Levodopa or DA-Agonists.
The objective of this lecture is to enable the participant to:

- Make an informed treatment selection for:
  - patients that present with fluctuating PD
  - Patient that are not adequately treated with oral therapies.

PARKINSON'S DISEASE - TREATMENT DEVELOPMENT FOR THE FUTURE

DIETER H. MEIER
CEO of Neuropore Therapies Inc., San Diego, USA

The goal of future treatments for Parkinson's Disease is to slow or halt the disease progression.
To date, such 'Disease Modifying' approaches suffered from a combination of draw-backs: (1) therapeutic agents targeting pathways were implicated with symptomatic relief, (2) with the possible exception of some imaging techniques the lack of validated biomarkers to measure disease progression, and (3).the misuse of this term for promotional activities. (4) Despite serious efforts the clinical differentiation of disease modifying and symptomatic properties has not been successful.

Alpha Synucleine (aSN) deposits are found in Lewy Bodies, the hallmark of PD and other Synucleinopathies. As with other misfolded proteins, it is likely that the microscopically detectable polymers are final deposits while earlier stages of aggregates –oligomers - are involved in the pathogenic process. In principle, several therapeutic approaches to interfere with the accumulation of misfolded proteins are at hand: (1) to eliminate or at least reduce the protein, (2) to interfere with its aggregation and/or (3) to enhance the clearance mechanisms. The first mechanism has been shown to be successful in humans through a high degree of reduction of aSN and A-beta via specific antibodies in PD and Alzheimer's Disease, respectively. In the latter, a clinical improvement of the patients' dementia could not be shown to date, and in PD the studies have not been performed yet. While the physiological role of aSN is currently not fully understood, to pursue the alternative, to interfere with the aggregation of potentially disease causing oligomers may be a viable therapeutic approach which is currently at very early stages of exploration in humans.

The objective of this lecture is to enable the participant to:
- Critically question proposed 'disease-modifying' treatments
- Give some insight in to alpha-synucleine-targeted research


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