CoPGr CURRICULAR CHAMBER
SUBJECTS PRESENTATION FORM

SUBJECT'S ACRONYM: **RNP5761**

SUBJECT'S NAME: Advanced Topics in Hereditary Neuropathies

CURRICULUM/AREA: Neurology/17140

FOCAL AREA: Neurology

INITIAL VALIDITY (Year/Semester):

N. OF CREDITS: 02

Theoretical Classes: 06 Practical Classes, Seminars and Others: 04 Hours of Study: 05
DURATION IN WEEKS: 02

PROFESSOR(S) IN CHARGE:
USP Professor, n. 93273 – Wilson Marques Junior

ACTUAL COSTS OF THE SUBJECT: BRL

(Presenting, if applicable, the budget foreseen for the year, as an attachment)

PROGRAM

OBJECTIVES:

1. Study of the Genotype and Phenotype Aspects of the Hereditary Neuropathies
2. Identification Methods of the Genes Responsible by the Hereditary Neuropathies
3. Physiopathology of the Myelinic and Axonal Hereditary Neuropathies
4. Perspectives of Curative Treatment of the Hereditary Neuropathies
5. Post-Genomic Studies

JUSTIFICATION:

The hereditary neuropathies are the most common nervous system's monogenic disease, with a prevalence estimated from 1 to 4 people attacked in each 10,000. Among the patients referred to tertiary neuromuscular centers with syndromic diagnosis of peripheral neuropathy without defined cause, the most common final etiology is the hereditary one. At he series from Dyck et al (1981), 42% of the referred patients received this diagnosis, at Barohn (1998)'s series, this value was 30% and at Singleton and Smith (2000), 43%. There are no studies in our country assessing the proportion of patients with neuropathy and undefined etiologic diagnosis which assessment results in the recognition of an hereditary neuropathy. The existent data indicate that these neuropathies represent around 15.5% (Marques Jr et al, 1992) and 8% (Freitas et al, 1990) of all the patients with peripheral neuropathy with defined etiology followed-up in two university hospitals, which implies in significant prevalence of these neuropathies in our third sector. In the last years, with the introduction of molecular biology techniques, a significant improvement occurred on the knowledge of these neuropathies (Shy et al, 2005). Currently, at least 33 different genes are known, and 50 different loci have already been identified, and it is expected that this number will be higher, since many families are not framed in any of these locations (Szigeti et al, 2006). If we include the neuronal CMT, currently best known as distal spinal muscular atrophy, these number will be even higher (Iroby et al, 2004). This genotype variability is associated to an enormous phenotype variability. Despite these troubles, the contributions of this molecular advance to the clinical practice of the hereditary neuropathies are numerous. The possibility of an accurate and unquestionable diagnosis is essentially important to the patients and their doctors, mainly to the ones without a family history of the disease. Since it is an extremely accurate, non-aggressive and economically accessible method, it enables a more objective assessment, preventing the performance of more aggressive methods, such as the nerve biopsy, or the performance of a large number of other laboratory examinations, which is unfeasible in most centers, even in economically privileged centers. Other

important contributions are the possibility of a grounded genetic counseling and the performance of predictive tests. The identification of the responsible genes has also allowed the study of these genes' function and the disease mechanisms of the resulting neuropathies. Experimental models with transgenic animals have been continuously developed and applied in the study of the development mechanisms of such diseases. Finally, all this advance has enabled the development of therapeutic possibilities (Hörst et al, 2006), and some clinical tests were or have been started, opening treatment perspectives to diseases that, predominantly, do not kill the patient, but they are associated to limitations which are many times important.

CONTENT (SYLLABUS):

Epidemiology, clinical evaluation, genotype-phenotype correlation:
1 - Neuroepidemiology Principles Applied to Peripheral Neuropathies
2 – Creation of a local, regional and national data bank of the peripheral neuropathies. Importance for the research. Wayne University Experience
3 – Current Classification of Hereditary Neuropathies
4 – Genotype Aspects of Hereditary Neuropathies
5 – Genotype-Phenotype Correlation. Phenotype Variability and Genotype Variability

Identifying Genes in Hereditary Neuropathies:
1 – The Genetic Mapping
2 – Principles of Genetic Links
3 – Studies of Genetic Links in Homozygous Diseases
4 – Genes' Identification Methods

Diagnostic Methods of Hereditary Neuropathies
1 – Importance of the Molecular Diagnosis for the Individual and its Family. Genetic Counseling
2 – Population Importance
3 – Duplication and Deletion Identification 17p11.2-p12
4 – Identification Methods of Other Mutations

Physiopathology and Treatment of the Hereditary Neuropathies
1 – Physiopathology of the Demyelinating Neuropathies
2 – Physiopathology of Axonal Neuropathies
3 – Investigating the Function of the Genes
4 – Reasonable Treatment Perspectives of the Hereditary Neuropathies

Migraine as Progressive Disease:
1 - From Episodic to Chronic Migraine - Clinical Characteristics, Epidemiology
2 - Risk Factors for Migraine's Progression
3 - Migraine's Physiopathology. Emphasis to the Interfaces with the Mitochondriopathies
4 - Progression Mechanisms. Progression Physiopathology
5 - New Frontiers- Migraine as Risk Factor to CVA, Coronary Disease and Demyelinating Lesions
6 - Drawing Clinical Studies for Investigating Migraine as a Progressive Disease

Clinical Method - Drawing a Randomized Clinical Study.
1 - Defining Medicine Based on Evidences - Principles
2 - The Randomized Clinical Study - Types and Phases
3 - Drawing Clinical Studies for the Acute Treatment of the Pain
4 - Drawing Clinical Studies for the Preventive Treatment of the Pain
5 - New Drawings - Studies Privileging the Recurrent Chronic Character of Migraine.
6 - The Headache Consortium Guidelines. The Evidence Translated to the Clinical Statistic Practice.

EVALUATION METHOD:

100% of presence weigh 2
Participation in seminars weigh 3
Practical Works weigh 3
Oral Evaluation weigh 2

NOTES: