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Transcriptional regulation of the human muscarinic M2 receptor gene

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Muscarinic M_2 receptors are important regulators of airway smooth muscle tone and alteration in M_2 receptor function has been described in asthmatic patients. Information regarding transcriptional regulatory control of muscarinic M_2 receptor expression in human airway smooth muscle cells is not available in the scientific literature.

This project aimed to study the transcriptional regulation of human muscarinic M_2 receptors and identify potential polymorphic variation, which may contribute to alteration in receptor expression.

Total mRNA was extracted from a human airway smooth muscle (HASM) primary cell culture and used as a template for analysis. A 5' RACE (Rapid Amplification of cDNA Ends) approach was used to identify and characterize the promoter region of the M_2 receptor. The promoter activity of pGL3E deletion constructs was subsequently investigated using a luciferase-based reporter gene assay approach in transiently transfected HASM and BEAS-2B cells.

Three different regions of transcriptional initiation were identified, with multiple transcription start sites (TSSs) clustered within each region. The distance separating the most 5' TSS from the coding region exceeds 146kb, and includes multiple exons, some of which are alternatively spliced. Sequencing of genomic DNA revealed the presence of a novel 0.5kb hypervariable region located 648bp upstream of the most 5' TSS, a CÆA SNP located 136bp upstream of the most 5' TSS and a multiallelic CA tandem repeat 96bp downstream of the most 5' TSS. The CA repeat has been shown to influence reporter gene transcriptional activity in transient cell transfectants.

This study has elucidated the arrangement of the muscarinic M_2 5' untranslated region, and has defined the key regions likely to be important in transcriptional regulation of the gene in HASM cells. Studies to define potential linkage between the functional tandem CA repeat and asthma are currently underway.

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Immunological levels in patients treated with new and old AEDs

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Studies have shown that many traditional antiepileptic drugs (AEDs) alter immunoglobulin (Ig) levels in patients and that immunological factors might contribute to the development of epilepsy. This study considered the effect on Igs, of therapy with traditional and newer AEDs, and a determination of the effect of selected AEDs on lymphocyte proliferation in vitro. In Study 1, group A patients (n = 16) were taking a combination of old and new AEDs. Group B patients (n = 12) were relying solely on old AEDs. Ten healthy volunteers served as a control group. Four blood samples were withdrawn from each patient at 3-month intervals. IgA, IgM and IgG levels were measured using an immunoturbidimetric procedure. In study 2, lymphocytes were extracted from healthy male volunteers and treated with increasing concentrations of vigabatrin (VGB), gabapentin (GBP) and phenobarbitone (PBT). Lymphocyte proliferation was measured using the liquid scintillation technique, and the results compared to untreated controls. In Study 1, the mean plasma IgA levels were lower for both group A and group B patients, compared to the controls, but not for IgM and IgG levels ($p<0.05$). The results obtained in the in vitro study showed that for the selected AEDs, there was an immunostimulatory effect in an incubated cell culture for 72 hours, at concentrations of 107pg/ml for VGB and GBP, and at a concentration of 105pg/ml for PBT ($p<0.05$). It would be preliminary from these limited results to state categorically that the selected AEDs will stimulate lymphocyte proliferation in vitro, as only three donors were used. There is definitely scope for the carrying out of further in vitro tests with respect to both spectrum of AEDs selected, and the number of donors recruited. The results also indicate that analysis of T-cell and B-cell interaction in epileptic patients should be undertaken.

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Measuring consumer perception of a health professional

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Evaluation of the impact of the intervention of health professionals on patient care by the consumer is now gaining relevance within quality care systems. The aim of the study was to examine the Maltese public perception of the community pharmacist.

A self-administered tool based on a quantitative system was developed. The tool assesses consumer satisfaction with advice and services provided by the community pharmacist, and analyses perception of the pharmacist as a health advisor.[1] Psychometric evaluation of the tool was undertaken prior to implementation in the study. Subsequently the tool was distributed to 576 consumers (males 41%, females 59%, average age 33 years, age range 16-71 years). The consumers were identified from the five districts in which Malta is subdivided. Statistical analysis was undertaken using Biomedical Data Package software.

The average perception score obtained was 76% (55%-99%). Consumers from the southeastern region had a higher perception of the pharmacist (79%) when compared to consumers from the other four districts ($p<0.05$). Consumers aged over 51 years had a higher perception (79%) of the pharmacist than consumers aged between 15 and 30 years (75%) ($p<0.01$). Skilled manual workers had the highest perception of the pharmacist (80%) whereas managerial and professional workers had the lowest perception of the pharmacist (73%-75%) ($p<0.05$).

The average perception of the pharmacist may be improved through the organization of health promotion activities in the community pharmacy setting. Such activities will enhance the professional aspect of a community pharmacy and will emphasise the availability of the pharmacist as a health advisor.

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Patient counselling on discharge

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Patients who are discharged after hospitalisation may have difficulty in understanding the correct use of medications. The aim of this study was to evaluate pharmacist intervention in counselling elderly patients upon discharge from an acute hospital.

A prospective, comparative study was undertaken at Zammit Clapp Hospital, an acute geriatric hospital. The pharmacists prepared four-day medicines supply and a discharge medication leaflet for patients discharged during a