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MED/09 Medicina interna

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CARRIERA ACCADEMICA: 1998-2000: Ricercatore confermato; 2000-2003: Professore associato non confermato; 2003-2006: Professore associato confermato, 2006-2009 Professore Straordinario.

INSEGNAMENTI. 1998-2009: Medicina d'urgenza, Immunologia clinica, Semeiotica medica, Fisiopatologia clinica; Terapia medica, Medicina Interna.

CURRICULUM. Dopo la maturità scientifica si laurea nel 1984 in Medicina e Chirurgia presso l'Università di Torino; ottiene nel 1986 una borsa di studio dall'Associazione Italiana per la Ricerca sul Cancro. Nello stesso anno soggiorna negli Stati Uniti presso il Wistar Institute di Philadelphia e in Svezia presso i laboratori del Dipartimento di Genetica clinica dell'Università di Lund. Nel 1987 consegue la specializzazione in Ematologia Generale (Clinica e Laboratorio). Nel 1988 soggiorna presso i laboratori del Department of Pathology, School of Medicine della Temple University di Philadelphia (USA). Nel 1989 ottiene una borsa di studio del Comitato Gigi Ghirotti, sezione Piemontese. Nel 1990 soggiorna presso i laboratori del Department of Pathology, School of Medicine della Temple University di Philadelphia (USA). Dal 1994 al 1998 è ricercatore presso la Clinica Medica, Dipartimento di Scienze Mediche della II Facoltà di Medicina e Chirurgia della Università degli Studi di Torino, sede di Novara. Nel 1998 ottiene un finanziamento triennale dall'Associazione Italiana per la Ricerca sul Cancro. Nel 2000 vince il concorso da Professore Associato di Medicina Interna presso l'Università di Modena e Reggio Emilia. Nel mese di ottobre, con chiamata della Facoltà di Medicina di Novara, prende servizio come Professore Associato di Medicina Interna presso la facoltà di Medicina e Chirurgia dell'Università del Piemonte Orientale. Nel 2003 gli viene conferita la responsabilità della Unità Didattica Assistenziale (UDA) Universitaria di Medicina d'Urgenza presso l'Ospedale Maggiore della Carità di Novara. Nel 2005 gli viene conferita la responsabilità della Struttura Complessa a Direzione Universitaria di Allergologia e Immunologia Clinica presso l'Ospedale Maggiore della Carità di Novara. Nel 2006 vince un concorso da Professore Ordinario presso l?Università di napoli, federico II, Nel mese di Novembre, con Chiamata della Facoltà di medicina e Chirurgia prende servizio come Professore Straordinario. È coordinatore dei Corsi integrato di Patologia Integrata Medica, di Semeiotica e Farmacologia. Insegna anche nella Scuola di specializzazione in Medicina interna (insegnamenti: Metodologia clinica, Ematologia, Medicina d'urgenza). Recentemente, 2009, è stato eletto direttore della Scuola di Specializzazione in Medicina d'Emergenza-Urgenza. Dal 2005 a tutt'oggi è Presidente del Corso di laurea in Infermieristica e dal 2006 è presidente del Corso di Laurea Magistrale in Scienze Infermieristiche ed Ostetriche.

CAMPI DI INDAGINE NELLA RICERCA. Ematologia sperimentale; immunologia; angiogenesi, infiammazione.

TEMI CORRENTI DI RICERCA. *Gas6 evaluation in patients with acute dyspnea due to suspected pulmonary embolism*. Gas6 protein is involved in pulmonary embolism (PE) and acute inflammation in animal models. METHODS: We enrolled 82 consecutive patients with acute dyspnea and suspected PE (Geneva score with high (HCP) or low/intermediate clinical probability (LICP)+D-dimer >or=0.5microg/mL) and 29 age-matched healthy volunteers. According to clinical and instrumental evaluations the following diagnoses were obtained: heart failure (HF), pulmonary or systemic infection (I), PE, or no illness (N). Twenty-two patients were excluded due to oral anticoagulation (9), lack of CT angiography or pulmonary scintigraphy (6), plasma creatinine >or=3mg/dL (3), and pulmonary cancer (4). Plasma Gas6 was measured with a validated enzyme-linked immunoassay. Non-parametric tests and accuracy measures were calculated. RESULTS: Out of 60 patients included, 8 were N, 12 HF, 11 I and 29 PE. Gas6 median value in the N group (20.4ng/mL, interquartile range 17.6-21.6) matched that of healthy volunteers, 19.1 (17.2-21.4). Median Gas6 values in HF, 26.4 (21.6-33.3) and I groups, 34.1 (30.0-38.7), were significantly higher than those in PE 18.2 (16.3-23.3) or N (Kruskal-Wallis test p<or=0.05) groups. Gas6 test improved PE diagnosis with an area under the curve of 0.80 and 0.91 (in all and LICP patients). A 24ng/mL threshold excluded PE in 33% of LICP patients without loosing any diagnosis. CONCLUSIONS: The data link Gas6 protein to infection/inflammation, but not to PE, in humans. Gas6 assay was useful in PE diagnosis, improving D-dimer accuracy particularly in LICP patients, and limiting GAS6 induces proliferation in prostate carcinoma cell lines expressing the axl receptor. Axl is a tyrosine kinase receptor and although it is expressed in malignancy such as leukemia, colon cancer, melanoma, endometrial, prostate and thyroid cancers, its role has not been completely elucidated yet and appears to be complex. The ligand of Axl, Gas6, is a 75 KDa multimodular protein with an N-terminal gamma-carboxy-glutamic acid that is essential for binding. Gas6 has a mitogenic effect on several normal cell lines. The receptor Axl is expressed in primary prostate carcinoma and in prostate cancer cell lines as such as PC-3 and DU 145. We demonstrated a mitogenic activity determined by Gas6/Axl interaction in these undifferentiated metastatic human prostatic cancer cell lines. This effect is proportional to Axl expression, not due to inhibition of apoptosis, and induces AKT and MAPK phosphorylation. However, only MEK phosphorylation seems to be essential for growth signaling. Our results suggest that Axl overexpression and activation by Gas6 could be involved in progression of prostate neoplastic disease.

Suspected acute allergic reactions: analysis of admissions to the Emergency Department of the AOU Maggiore della Carità Hospitalin Novara from 2003 to 2007. The aim of our work is to ascertain the frequency and the impact of acute allergic reactions on the routine of a highly-specialized Emergency department collecting information on the admission, the typology of symptoms and the degree of severity calculating the incidence and the outcomes of the events. MATERIALS AND METHODS: The study started the 1 July 2006 and the records of the Emergency Department of the

Maggiore della Carità Hospital in Novara were consulted retrospectively in the period between the 1 January 2003 and the 31 December 2006, and prospectively up to the 31 December 2007, using keywords that could identify admission for suspected allergic reactions. Information relating to internal medicine and/or pediatric cases were examined, excluding all surgical and/or trauma cases. The number ofadmissions per year was considered broken down by clinical signs, triage assessment upon admission and discharge outcome. RESULTS: Admissions to the Emergency Department during the period under consideration were 165,120 with 6107 suspected cases of allergic reactions. The symptoms most frequently reported both in adults (A) and children (C < or =18 years old), were: hives 37%, asthma 20.65 (A)% and 27.4% (C); drug allergy 7.5% (A) and 6.1% (C). Reactions to Hymenoptera venom were less frequent, 4.7% (A) and 1.27% (C); the frequency of angioedema, conjunctivitis and rhinitis was between 1 and 4%. The incidence of food allergies (1.4%) and anaphylaxis (0.8%) was comparable for all ages. The triage assessment showed a significant percentage of "yellow" and "red" codes, with 362 cases (5.9%) and 71 cases (1.16%) respectively. A total of 151 patients was hospitalized, no one classified as "white" code. Death occurred in 7 cases: 4 "yellow" codes and 3 "red" codes, respectively. A more detailed specialistic evaluation was recommended in only 10% of the patients. CONCLUSIONS: Admissions to the Emergency Department for suspected allergic reaction are proportional to the number of overall admissions for internal medicine cases and do not appear to be related to the general increase of allergies in the population. This led us to focus our attention on how allergic diseases impact the work of an Emergency Department and how to describe the discharge diagnosis better. A significant number of descriptive diagnoses also turned out to be inaccurate and did not allow the syndrome to be identified properly. The analysis of this information aims to be a stimulus to improve the emergency clinical approach used for allergic diseases and to plan the adequate management ofallergic patients after they have been treated in hospital.

*Development and validation of an ELISA method for detection of growth arrest specific 6 (GAS6) protein in human plasma.*Gas6 protein is possibly involved in human diseases, but a validated plasma assay is lacking. So, we developed a sandwich enzyme-linked immunosorbent assay (ELISA) method using commercially available reagents. An appropriate plasma-based matrix was prepared to optimize the assay. The ELISA method showed inter- and intra-assay coefficients of variation lower than 15%. Recoveries all fell within 15% of expected values. Plasma Gas6 concentration in 61 healthy donors was 20.3+/-3.8 ng/mL. Our assay meets FDA requirements for precision and accuracy for the validation of bioanalytical methods and it is suitable for research or diagnostic purposes.

Inhibition of vascular endothelial growth factor receptor 2-mediated endothelial cell activation by Axl tyrosine kinase receptor. GAS6, the product of a growth arrest specific (GAS) gene, is the ligand of the tyrosine kinase receptor Axl. GAS6 and Axl are both expressed in endothelial cells, where they are involved in many processes such as leukocyte transmigration through capillaries and neointima formation in injured vessels. Here, we show that Axl stimulation by GAS6 results in inhibition of the ligand-dependent activation of vascular endothelial growth factor (VEGF) receptor 2 and the consequent activation of an angiogenic program in vascular endothelial cells. GAS6 inhibits chemotaxis of endothelial cells stimulated by VEGF-A isoforms, but not that triggered by fibroblast growth factor-2 or hepatocyte growth factor. Furthermore, it inhibits endothelial cell morphogenesis on Matrigel and VEGF-A-dependent vascularization of chick chorion allantoid membrane. GAS6 activates the tyrosine phosphatase SHP-2 (SH2 domain-containing tyrosine phosphatase 2), which is instrumental in the negative feedback exerted by Axl on VEGF-A activities. A dominant-negative SHP-2 mutant, in which Cys 459 is substituted by Ser, reverted the effect of GAS6 on stimulation of VEGF receptor 2 and endothelial chemotaxis triggered by VEGF-A. These studies provide the first demonstration of a cross talk between Axl and VEGF receptor 2 and add new information on the regulation of VEGF-A activities during tissue vascularization.

PUBBLICAZIONI PIÙ RECENTI.

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