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## Preface

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*Dear Colleagues,*

this volume contains the proceedings of the Third "International Conference on Thrombosis and Hemostasis Issues in Cancer", held at the Congress Center Giovanni XXIII, in Bergamo, Italy, 14-16 October, 2005. The first two conferences, held in 2001 and 2003, grew progressively in stature and were well attended by delegates from all over the world. For this reason and because the field of thrombosis and hemorrhage in malignancy continues to grow rapidly, we consider it important to convene again and discuss the novel results and ongoing progress.

This conference focuses on translational research, with a strong balance between basic and applied research. We will hear from our colleagues who have for the very first time demonstrated that activation of blood coagulation in cancer is a direct result of oncogenic transformation. And we will use that information, perhaps, to consider new strategies that inhibit activation of both oncogenes and blood coagulation. At the last conference we centered much of our discussion on the hemostatic system imbalance associated with malignant disease. This imbalance underpins the characteristic thrombotic and hemorrhagic diatheses that occur commonly in these patients. We now know that activation of clotting and the resultant thrombosis and consumptive coagulopathy that can occur are not just complications of cancer that contribute significantly to the morbidity and mortality of this disease. Indeed, tissue factor expression, thrombin generation and other protease activation sequences linked to blood clotting, platelet function and fibrinolysis are primary to the malignant process and reflect the basic biology of cancer. Attacking these pathways is becoming more germane to the design of targeted therapy in cancer but such approaches may not always be straightforward. For example, inhibitors of angiogenesis, growth factors and other biological agents used to

treat cancer patients, may inadvertently activate blood coagulation and cause thrombosis and/or bleeding. Although bleeding syndromes are relatively rare in cancer patients, when they occur, they can be severe and life-threatening.

The association between cancer and thrombosis, which has been known for more than a century, is growing in importance and complexity. Giancarlo Agnelli, in his excellent review for the International Society of Thrombosis and Haemostasis just 8 years ago, titled his presentation "Venous thromboembolism and cancer: a two-way clinical association" (Thromb Haemost 1997;78:117-120). He referred of course to the increased frequency of thrombosis in cancer patients and the increased frequency of an occult cancer in patients with idiopathic venous thromboembolism. But we are now faced with a much more complex set of associations, in which oncogenic events activate clotting, clotting proteins interact with tumor cells to enhance cell movement, growth and angiogenesis, as well as providing a substratum for tumor implantation and growth. Platelets, endothelial cells and fibrinolytic proteins facilitate tumor cell interactions and locomotion. Naturally occurring anticoagulants, including heparin-like mucopolysaccharides, provide important reservoirs of growth factors for tumor cells and tumor-associated heparanases may be important targets for novel approaches to cancer chemotherapy.

On the basis of this new understanding of pathological thrombus formation in cancer, novel approaches to antithrombotic therapy have been developed with some intriguing early successes. Exciting data from several of the more recent clinical trials are presented, which have changed the clinical practice of antithrombotic therapy in cancer patients and may revolutionize anti-tumor therapy as we know it. Pre-clinical and clinical investigations on the anti-tumor effects of antithrombotic drugs are in rapid progress and some of the early suc-

cesses of this approach are discussed.

The aim of the conference is to review recent advances in basic and clinical research; both prevention and treatment strategies of thrombohemorrhagic complications in cancer patients are extensively reviewed. Our wish is to continue to bring together leading researchers and clinicians and the format of the Conference is designed to favor an active exchange of important information and topics of research and to provide stimulation for cross-disciplinary collaborations.

The sessions of this conference cover a number of different issues, including: 1. Epidemiology and Patho-

genesis of Thrombosis in Cancer; 2. Experimental Models of Clotting/Tumor Interaction; 3. Antithrombotics and Fibrinolytics and Cancer Survival; 4. Endothelium Targeting and Anticancer Therapies; 5. Bleeding and Inflammation; 6. Glycosaminoglycans, Cancer and Thrombosis; 7. Recent Advances in the Prevention and Treatment of Venous Thromboembolism in Cancer.

We sincerely hope that this volume will serve as an up-to-date review of this rapidly changing field, while stimulating new ideas and collaborations between basic and clinical investigators.

We wish to thank all participants for their contributions.