# In memoriam of Prof. Armando D'Angelo (1952-2024)

## Armando, we've known each other well for 40 years

I set out to write these brief notes, which will serve as the introduction to the present Issue of *Bleeding Thrombosis and Vascular Biology* dedicated to Armando D'Angelo, with mixed feelings. On the one hand, it does not come naturally to me to write formally about a colleague and a brotherly friend, when I would rather speak to his soul. A soul that Armando never tried to hide from those who were close to him. A soul that allowed him—but above all allowed those who knew him—to connect with him instantly.

On the other hand, I would like to list the extraordinary wealth of scientific contributions that established him as one of the most accomplished figures in the field of hemostasis and thrombosis, through timely and erudite interventions at the many occasions we had to meet, and through a body of high-level scientific work.

The truth is that these two sides of him coexisted harmoniously. In any case, I could not remember Armando without speaking of his heart, sincerely inclined toward sharing and true friendship.

I therefore leave it to others to outline his scientific merits and allow myself the freedom to speak to him as if he had never left. Below I include what I wrote to him on the day that upended my life and that of many others. Next to my letter to Armando, you will find what Chuck Esmon, Armando's mentor and brotherly friend, told us at the national SISET congress in Rome in 2024. Over the course of 2026 we also lost Chuck, the longtime co-organizer with us of the Winter Meetings, whose death was preceded by a few months by the passing of his beloved wife, Naomi Esmon, the faithful heart and soul of all our Winter Meeting gatherings.



Armando D'Angelo (1952-2024).

*March 13, 2024*
*From: Armando D'Angelo <...@hsr.it> Wed, 13 Mar, 07:15 AM To: Franco Piovella*
*Thank you, Franco. Today they're performing a TAVI on me. Let's hope to speak again soon. Armando*

*From: Franco Piovella <...@gmail.com> Tue, 13 Mar, 08:37 AM To: Armando D'Angelo*
*Today I'm with you. See you just outside. Franco*

Hello, dear Armando.

I can hardly see what I'm writing—since yesterday there's been a veil of tears before my eyes.

I've rewritten here the last words we exchanged that last morning, to make sure it all truly happened. And so quickly.

We usually worried about being late with some work, or with the Winter Meeting program—never about the idea that we might not be untouchable: each with our own problems, but somehow immortal. And then you wrote to me "Let's hope to hear from you again".

I'm writing these words because I feel you can somehow read them—or feel them coming from my soul.

We've known each other well for 40 years. We were at ASH in Washington, 1985… You were coming from Oklahoma City and heading back to Milan. Since then, through many circumstances, we worked almost side by side. For a year, after my retirement, we truly did so at San Raffaele Hospital.

And beyond work, we always loved sharing time and ideas. Never holidays. I have never given up on vacations; you never wanted to take them. You're too good, curious, and intelligent; you loved your job and considered holidays a kind of "wasted time," dedicated to doing nothing. So, we reached a conclusion: to share the moments our temperaments demanded, we had to invent what didn't exist—a serious job, on vacation.

And we did it. For more than 20 years, we built the bi-annual editions of our International Winter Meeting on Coagulation. You turned it into a mark of quality. Our important friends—accustomed to international meetings with thousands of delegates—came and asked to be invited, and invited again, to our gathering of no more than a hundred participants. And what participants! The best scientists around. For a week in the mountains, we made them feel at home: in the morning, breakfast in pajamas, then straight to work. And what special guests we managed to bring for moments beyond our science! In the evenings, after the last scientific session, we drew out of each delegate what they didn't know they had inside. Do you remember? You even had a future prime minister sing karaoke for us!

Armando, it felt like a Renaissance court hosting the very best artists in its halls. And we didn't pay them…

Then, as always, everything gradually dissolved—partly because the once-immature researchers had matured, partly because the circumstances changed.

I've written these lines of history because they let me tell the shared things that filled us with joy and pride—and, above all, because doing so has kept me from crying.

Now I return to speak to you, my great friend. You know that sometimes I see in you an older brother, wiser than I am, though I'm the older one. And you call me "Franchino." You manage to temper my character when it gets a bit too reactive.

And you were the only one who, when my father passed away, could write me a wonderful letter.

You're the only person who can make people laugh—friends or mere acquaintances—while saying things that, from others, would sound like insults and inflame the recipients. You sweeten them. And you make people love you.

You are the soul of every meeting, scientific or otherwise. Everyone knows your powerful spirit and your smile.

These lines are a poor substitute for that "see you" I wrote to you. But I choose to think that that day we truly saw each other. And we will go on seeing each other, as always, and speaking soul to soul—and I know you will hear me and help me in difficult times.

Goodbye, Armando—my great, intelligent, cultured, ironic, generous, and kind friend. I'm sure that where you are, there's a place to hear your beloved music at its very best (never mind hi-fi stereo…).

I have to say goodbye now, because I truly can't see the words anymore.

Your Franchino

**Franco Piovella**
IRCCS Istituti Clinici Scientifici Maugeri, Pavia, Italy

## Armando combined scientific and professional skills with a human trait of great hospitality and courtesy

Prof. Armando D'Angelo passed away on March 14, 2024, suddenly after a cardiac invasive procedure. Armando focused on the field of blood coagulation and thrombosis and people who had the chance to work with him were captured by his real passion for clinical and laboratory research.

Armando was born in Milan in 1952 where he graduated Doctor of Medicine in 1977 and subsequently specialized in Internal Medicine.

He visited Oklahoma City in close contact with Doctor Chuck Esmon for some years, and in 1985 he returned to Italy with a strong commitment to research on congenital and acquired thrombophilic states, on sepsis and on homocysteine metabolism. Since then, he served as Director of the Coagulation Service and Thrombosis Research Unit of the IRCCS San Raffaele Hospital in Milan.

Armando's career was characterized by an impressive scientific production of more than 250 contributions in the area of congenital and acquired thrombophilias and in the development of new analytic methods.

His clinical research activity has always been supported by a particular and very solid laboratory expertise, a reflection of a deep knowledge of the mechanisms of hemostasis. Those who listened to him exposing the results of his research were transported into a complex world full of intuitions and pathophysiological connections, but never getting lost, but always accompanied by a careful and rigorous guidance.

He has been involved in the standardization of blood coagulation tests as Chairman of the Working Group of the International Federation of Clinical Chemistry (IFCC) and in the ISTH. He has also been present in the Board of Directors of the FCSA and SISET, and has assumed the position of President of SISET in the two-year period 2013-2014. Since 1988 he was the Director of the Coagulation Service and Thrombosis Research Unit of the IRCCS San Raffaele Hospital in Milan, always available, as he wrote in his profile, to provide a clinical judgment about the required tests and possibly to suggest the development of the diagnostic procedure, in a perfect synthesis between clinical and laboratory skills.

He combined scientific and professional skills with a human trait of great hospitality and courtesy; with him you always felt at ease. Armando demonstrated how to achieve excellence in one's work without losing the joy of friendship and fun. *Bel canto*—the opera he loved so dearly—reflected his character, for singing well also requires discipline. His smile and generosity have forever enriched our community. His memory will continue to inspire us.

**Valerio De Stefano**
Past President of the Società Italiana per lo Studio dell'Emostasi e della Trombosi (SISET)
Università Cattolica del Sacro Cuore, Fondazione Policlinico A. Gemelli IRCCS, Rome, Italy

## Reminiscences from the mid-Eighties and the first example of protein C and activated protein C to treat sepsis

Here I will tell you some reminiscences of Armando. It was my great pleasure to have him apply to my laboratory. We were in the mid-Eighties and I was updating professors. He said he wanted to learn how to purify proteins and work with enzymes and so forth. Sure, I said, come on!

So he did and we did, and we played around in the laboratory quite a bit. From the first time that he showed up in the laboratory I was quite convinced he was going to be pretty successful career wise. He was only a baby professor, so it was not clear at that time that he was going to be successful, but I thought he was. And by God, how awfully was. He developed interests in fibrinolysis and bleeding complications, hemostasis, thrombosis, sepsis. And that was kind of fun because those were all the things that I was interested in too. We actually did share the scientific bond there and we played around by the lab and talk about what we thought was going on. In my case, I was often wrong, but he was often right.

Once he established these areas of expertise, he started working in my laboratory. Armando dedicated himself to isolate proteins. We had this great big column two to three meters tall.

Before I tell you this story, I have to tell you something else about Armando. He ran on European time. He never did switch to the US time. In my case, when I knew I was having a long day, I came in early. And Armando? No, one o'clock, two o'-clock in the afternoon he would show up. And at first, since this was exactly the opposite of my own approach, it was driving me crazy, I thought, what in the world are you doing? Turned up? He didn't mind it at all. And he could carry on overnight.

Anyway, we made this concoction. Loaded it on this column. When it was time for me to go home, Armando was just getting started. When I came in the next morning pretty early, I went to the cold room. There was the column, but there was no running down the column, and long strings coming down. That became an ongoing joke in the lab, because I call that "the famous *linguine* column".

But he pursued and eventually got to the point where he's pretty decent at isolating proteins. Never made any more *linguine* columns either.

About the same time this was all going on, in the lab we have been working on this sepsis problem, and to get the paper finished we had to get references for protein C and activated protein C and everything else because the referees for journals want you to get all sorts of data that are available. So, we had to develop those. Well, that was Armando's job. And he fully participated to the writing of the paper which was the first example of protein C and activated protein C used to treat sepsis, and Armando was instrumental in that.

Those are the types of really enjoyable things that we had, and they set up the interactions we had for a long time. And he made very much fun for everybody in the laboratory when he was here, because it was a different view of the world. And he was always happy.

Armando marched to his own rules. So, there was this thing on smoking and non-smoking. He absolutely did not pay any attention to those rules. But he did it with a smile on his face everybody seemed to think that was OK, I guess.

He then established enough of a presence that he was able to work with Franco Piovella to set up this International Winter Meeting on Coagulation, that I think was probably his biggest contribution during his scientific career. Now this was from my perspective, it was kind of fun because I got invited to be part of the Scientific Committee, and so it was my chance to go to Italy and have a very good time, all the time. And I was also given the privilege of being able to identify who was doing something that was interesting in the States, and try to invite him over to the meeting. That was the easiest job I've ever had because all I had to do was to say: "We've got this Winter Meeting going on in Italy, in the mountains, would you like to come and give a talk?" Well, scientists are very busy people, but I never got burned down, they all said: "Yeah, I'll do it, and I'll check my schedule for what I'm having to cancel". At the International Winter Meeting we exchanged science with investigators from all over Italy and investigators from the States and from other different Countries. I think we all learned a great deal, especially the clinical sciences, which are relatively weak in the States whereas more biochemical approaches are fairly strong.

Armando came to my place, and he was going to stay, I think, for six months or something like that. Eventually he did stay for three years and we had a lot of fun.

Just to add a story, which is not so much science, but kind of fun: we had a boat and there was a lake and a little island on the lake. I did take Armando up there; he liked the place a lot. And we went up one day in the middle of the summer. In Oklahoma, in summer it never rains, and then it's almost always dry. That day, as soon as we took off, it rained as a banshee and rained and rained. Then he said: "Ha, I've been here for many years, it never rained on me. Today it rained twice. I can't stand this". So that was the end of that trip, but that was just kind of the fun types of things that we did, and it was really an enjoyable time.

I learned a lot from Armando, especially the clinical aspects of the medicine, and he learned a few things from me. I'll miss him very much. He was a really great guy. Thank you very much again, Armando, for all those wonderful things we had together.

**Charles "Chuck" T. Esmon**
Oklahoma Medical Research Foundation
(passed away on May 1, 2026).



Armando, Chuck and Naomi in the mid Eighties, at Oklahoma City.

## "Stiamo in gruppo!" ("Let's stay together")

I consider myself extremely blessed and lucky to have met Armando D'Angelo in 2008 in Italy during a bi-annual conference on Thrombosis and Hemostasis that he and Franco Piovella coordinated together, the International Winter Meeting on Coagulation. The conferences absolutely enveloped one of his favorite sayings - "Stiamo in gruppo!!" ("Let's stay together") – referring to scientific colleagues and friends working together from multiple Countries, but also knowing how to have fun together even after the science and learning. The conferences were unique and invited the world's best physicians, clinicians and laboratory experts to bridge the gaps between teams and individuals of various disciplines and open new discussions on research ideas and collaboration that continue to synergize international research from experts around the world.

The conferences were extremely interactive with colleagues often being challenged even during presentations because clinicians knew each other so well. I remember Armando challenging one of my points during a presentation on the prevention of venous thromboembolism in medical patients and the varying efficacies of low molecular weight heparins in this population. It was a great learning moment for me and I acknowledged that he indeed was correct and I made a false deduction. He gave me this advice in a positive, yet of course critical, fashion that I still appreciate today and took down the road to later lectures.

These conferences bridged gaps better than most conferences because of the open discussions before, during and after the events. It was both Armando and Franco's leadership styles that worked so well together to create such a great learning environment.

Armando always had a smile on his face and a bellowing laugh that I will never forget. I still remember him as if it was yesterday, singing Andrea Bocelli's songs, sounding as good as the famous opera singer himself. I will also always remember his contagious laughter and unbelievably quick wit. Armando could entertain a group of hundreds with jokes and humor endlessly without effort or hesitation – it came to him so naturally. One of my fondest memories was Armando rallying a group of people with Franco around midnight to walk to an old Italian underground bar built out of stone in La Thuile, Aosta Valley, where everyone sang and drank from the "Coppa dell'Amicizia" ("friendship cup") for several more hours despite early morning presentations the next day… It is these important moments and memories that bring people from different Countries and continents together to better understand one another and build lifelong friendships and relationships despite missing some sleep.

Armando always had me laughing so much that my belly hurt and tears often rolled from my eyes from laughing too hard from his jokes whether it was day or night. I will always cherish my memories of him - his great smile, his great humor, his great heart, and him being such a great person. I will also always remember Armando's songs and voice echoing throughout and even outside of the hotel and his voice will carry on with my frequent, fond memories of the years and time I was able to spend and cherish with him.

Thank you, Armando, for being such a great friend and such a positive influence on my life and I look forward to seeing you on the other side.

**Charles "Kurt" Mahan**
University of New Mexico Health Sciences Center, Albuquerque, New Mexico, USA

## Excerpts from some submission letters

I loved the beauty of the Winter Meetings Franco and Armando chaired as a "Renaissance Court", where both brought the greatest international minds of thrombosis together in the same room, doing the same activities, socializing, and creating a perfect fertilization of cross-pollination for future projects and bold new ideas (i.e. remember the idea of LMWH as a pleiotrophic agent to possibly improve mortality in cancer-associated thrombosis).

The reason for the Winter meetings was to mix yours and colleagues loves of science/work/the beautiful outdoors and skiing.

**Alex Spyropoulos**
Northwell Health, New Hyde Park, NY, USA

Excellent idea to give credit to Armando's life and work. Like many, I also have memories of him! Some time ago, we were in Bergamo for ICTHIC and I never forget having co-chaired with Armando a session. Prior to this session, I met him sitting at a terrace in the street with a smoke and a beer and urging me to join him, as we still had "a lot of time" before this meeting would start… actually only 5 minutes… typical! On occasion he also used to tell us that we "Dutch should speak up, you are always so soft voiced" (whereas we always consider ourselves all speaking too loudly…). And "the only decent coffee in the morning is "ristretto", of course, "espresso" is for tourists".

A great guy, I think we all miss him and his abundant presence!

**Hugo ten Cate**
Maastricht University, the Netherlands

When I think of Armando, I fondly remember when I first met him on the "piazza" of the sun- drenched Italian ski valley in Bormio with his big smile and warm welcome to Italy. Armando projected booming laughter and possessed an engaging personality that drew in anyone lucky enough to encounter him. Armando's contributions to science have been invaluable and will live on for future generations. He will be dearly missed by all.

**Stefanie Mahan**
Presbyterian Healthcare Services, Albuquerque, NM, USA

I acknowledge the great wisdom, cheeriness, generosity, and scientific drive of Armando D'Angelo, to whom this work is dedicated, as well as Franco Piovella, who commissioned this work.

**Bruce L. Davidson**
Washington State University Floyd College of Medicine, Everett, WA, USA

Armando was an outstanding and highly insightful clinician-scientist whose personality truly was larger than life. His presence lit up any room he was in, and I especially appreciated his kindness and good-heartedness. I will forever have fond memories of interacting with him at those excellent International Winter Meetings on Coagulation. They were special meetings, and he was a special person. Our brief manuscript "Trypsin is at least as procoagulant as factor XIIa" reports some experiments we did that compare the relative clotting activity of enzymes in the contact pathway versus those in the intrinsic pathway & the final common pathway of blood clotting. We found the results thought-provoking and I think Armando would have found the study interesting.

**Jim Morrissey**
University of Michigan Medical School, Ann Arbor, MI, USA

We are pleased to dedicate our manuscript entitled "The Expanded Universe of Thrombin: A Comprehensive Review of Its Extra-Hemostatic Roles and Structure–Function Relationships" for consideration as a Review Article in *Bleeding, Thrombosis and Vascular Biology*, to the memory of Armando D'Angelo.

We believe that our work is particularly appropriate for this Issue, as it reflects the spirit of scientific rigor and translational relevance that characterized D'Angelo's contributions to the field of hemostasis and thrombosis, by bridging fundamental biochemical mechanisms with clinical perspectives.

**Raimondo De Cristofaro**
Università Cattolica Sacro Cuore, Roma, Italy

I am honored to submit a paper honoring the memory of Armando, a paper related to tissue factor pathway inhibitor (TFPI) and its interaction with the cofactors FV-Short and protein S. We provide insights into the structure-function relationships between the three proteins. Armando was very interested in the regulation of blood coagulation and in particular protein S and its role as regulator of the protein C system. He would have found the paper appropriate and suitable for this special issue.

**Björn Dahlbäck**
Lund University, University Hospital, Malmö, Sweden

The manuscript entitled "Whole exome sequencing in a family with thromboangiitis obliterans" stems from cooperation with Armando and his group, aimed at investigating genetic components that may confer susceptibility to thromboangiitis obliterans (TAO).

**Francesco Bernardi**
University of Ferrara, Italy