CURRICULUM VITAE

1. *Name:* **Aleksandra Antovic**

2. *Date of birth:* **February 17, 1974** *Personnr.* **740217-7880**

3. *Address:* **Huvudstagatan 33, 171 58 Solna**

Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology D2:01, 171 57 Solna

4. *Phone:* + 46 734294448

E-mail: aleksandra.antovic@ki.se

5 COURSES AND DEGREES

2012-2017: Specialization Rheumatology clinic, Karolinska University Hospital, Stockholm, Sweden

2011: Swedish medical licence

2008: Swedish medical exam

1999-2000: Master studies in biochemistry: Faculty of Medicine, Nis, Serbia. 1 year.

1999-2000: General Internship, Clinical Medical Centre Nis, Serbia

1992-1999: Undergraduate medical studies: Faculty of Medicine, Nis, Serbia; average mark 9.2 (6.0-10.00).

6 DOCTORAL DEGREE

2001 - 2004: PhD studies at Coagulation Research, Dept. of Molecular Medicine & Surgical Sciences, Karolinska Institutet, Stockholm, Sweden. PhD thesis: "Determinations of the Overall Haemostasis Potential and Fibrin Gel Permeability. Method development and application in research and in clinical materials" defence June 2004. Supervisor: Med Dr He Shu, co-supervisors, Professor Margareta Blombäck, Assoc. Professor Katarina Bremme.

7 POSTDOC APPOINTMENTS

2006 - 2008: Postdoc at Karolinska Institutet, Department of clinical sciences, Danderyd Hospital, funded by a postdoctoral stipend from David & Astrid Hagelens Stiftelse, KI. Project: "Hemostasis in diabetes mellitus in relation to gender; focus on coagulation and fibrin network formation and effects of aspirin".

2004 - 2005: Post-doc at the Department of Angiology, University Medical Centre, Ljubljana, Slovenia. Project: "Peptidomimetics – the inhibitors of coagulation activation and platelets aggregation". Funded by the Science and Education Foundation of the Republic of Slovenia.

8 DOCENT-LEVEL COMPETENCE

2015: Docent in Coagulation research, Karolinska Institutet, Deptartment of

10 PRIOR POSITIONS

March 2009 – December 2011: General-research Internship at Danderyd Hospital and Karolinska Institutet, Dept of clinical sciences, Stockholm, Sweden.

September 2008 – February 2009: Physician at Department of Medicine, Danderyd

KAROLINSKA INSTITUTET
SCIENTIFIC PORTFOLIO

1 CURRENT SCIENTIFIC ACTIVITY

Researcher at Karolinska Instituet, Dept. of Medicine, Solna, Division of Rheumatology in the group of Prof. Anca Catrina with 20% research time financed by the ALF-foundation. (http://ki.se/people/aleant)
Evaluation of different biomarkers of coagulation and fibrinolysis as possible predictors of venous thromboembolism and cardiovascular disease in autoimmune inflammatory diseases is in focus of my research.

2 SCIENTIFIC PUBLICATIONS

2.1 Bibliometric parameters

Number of peer-reviewed original publications: 32

Number of peer-reviewed review and editorial publications: 3

Number of other (book chapters, overview papers in Swedish) publications: 2

Total number of citations: 589

Sum of Latest Known Journal Impact Factor: 108.1

h-index: 14

2.2 List of all original works

Original publications in PhD thesis.

1) He S, **Antovic A**, Blombäck M. A simple and rapid laboratory method for determination of haemostasis potential in plasma II. Modifications for use in routine laboratories and research work. Thromb Res 2001; 101:355-361. PMID: 11553368

   http://www.ncbi.nlm.nih.gov/pubmed/11553368

2) **Antovic A**, Blombäck M, Bremme K, He S. The assay of overall haemostasis potential used to monitor low molecular mass (weight) heparin, dalteparin treatment in pregnant women with previous thromboembolism. Blood Coag Fibrinolys 2002; 13:181-6. PMID: 11943930

   http://www.ncbi.nlm.nih.gov/pubmed/11943930

3) **Antovic A**, Blombäck M, Bremme K, van Rooijen M, He S. Increased hemostasis potential persists in women with previous thromboembolism with or without APC resistance. J ThrombHaemost 2003; 1:2531-5. PMID: 14675088

   http://www.ncbi.nlm.nih.gov/pubmed/14675088

4) **Antovic A**, Perneby C, Jacobsson Ekman G, Wallen NH, Hjemdahl P, Blombäck M, He S. Marked increase of fibrin gel permeability with very low dose ASA treatment.Thromb Res 2005; 116:509-17. PMID: 16181986

   http://www.ncbi.nlm.nih.gov/pubmed/16181986

5) **Antovic A,** Blombäck M, Sten-Linder M, Petrini P, Holmström M, He S. Identifying hypocoagulable states with a modified global assay of overall haemostasis potential in plasma. Blood Coag Fibrinolys 2005; 6:585-96. PMID: 16269934

http://www.ncbi.nlm.nih.gov/pubmed/16269934

6) He S, Cao H, **Antovic A,** Blombäck M. Modifications of flow measurement to determine fibrin gel permeability and the preliminary use in research and clinical materials. Blood Coag Fibrinolys 2005, 16:61-67. PMID: 15650548

http://www.ncbi.nlm.nih.gov/pubmed/15650548

Original articles prior to PhD thesis.

1) Antovic JP, **Antovic A**. Does recombinant factor VIIa, apart from overall hemostasis, regulate TAFI dependent fibrinolysis? - In vitro analysis using overall hemostasis potential (OHP) assay. Thromb Haemost 2003, 99:620-627. PMID: 14515182

http://www.ncbi.nlm.nih.gov/pubmed/14515182

2) Antovic JP, **Antovic A**, He S, Tengborn L, Blombäck M. Overall haemostatic potential can be used for estimation of thrombin-activatable fibrinolysis inhibitor-dependent fibrinolysis in vivo and for possible follow-up of recombinant factor VIIa treatment in patients with inhibitors to factor VIII. Haemophilia 2002; 8:781-786. PMID: 12410647

http://www.ncbi.nlm.nih.gov/pubmed/12410647

3) Antovic JP, Rafik Hamad R, **Antovic A**, Blombäck M, Bremme K. Does thrombin activatable fibrinolysis inhibitor (TAFI) contribute to fibrinolysis impairment in patients with preeclampsia and/or intrauterine fetal growth retardation.Thromb Haemost 2002; 88:644-647. PMID: 12362237

http://www.ncbi.nlm.nih.gov/pubmed/12362237

4) Antovic JP, Östenson CG, Yngen M, **Antovic A**, Wallen H, Jorneskog G, Blombäck M. Thrombin activatable inhibitor (TAFI) and hemostatic changes in patients with type I diabetes mellitus with and without microvascular complications. Blood Coag Fibrinolys 2003, 14:551-556. PMID: 12960608

http://www.ncbi.nlm.nih.gov/pubmed/12960608

5) Antovic JP, **Antovic A**, Sten-Linder M, Wramsby M, Blombäck M. Overall Haemostasis Potential (OHP) assay – a possible tool for determination of hypercoagulable pattern in XII deficiency. J ThrombHaemost 2004, 2:2058-60. PMID: 15550050

http://www.ncbi.nlm.nih.gov/pubmed/15550050

Original articles after PhD thesis.

1) Vedin J, **Antovic A**, Ericsson A, Vaage J. Haemostasis in off pump compared to on pump coronary artery bypass grafting – a prospective, randomized study. Ann ThoracSurg 2005; 80:586-93. PMID: 16039210

http://www.ncbi.nlm.nih.gov/pubmed/16039210

2) Anzej S, Bozic M, **Antovic A**, Peternel P, Gaspersic N, Rot U, Tratar G, Stegnar M. Evidence of hypercoagulability and inflammation in young patients long after acute cerebral ischaemia. Thromb Res 2007; 120:39-46. PMID: 17034835

http://www.ncbi.nlm.nih.gov/pubmed/17034835

3) Rooth E, Wallen NH, **Antovic A**, von Arbin M, Kaponides G, Wahlgren N, Blombäck M, Antovic JP. Thrombin Activatable Fibrinolysis Inhibitor (TAFI) and its relationship to fibrinolysis and inflammation during the acute and chronic phase of ischemic stroke. Blood Coag Fibrinolys 2007; 18:365-370. PMID:17473579

http://www.ncbi.nlm.nih.gov/pubmed/17473579

4) **Antovic A**, Jörneskog G, Wallen NH. Comparison of two laboratory assays for the investigation of fibrin gel porosity. Thromb Haemost 2007; 98:1386-1388. PMID:10864345

http://www.ncbi.nlm.nih.gov/pubmed/18064345

5) Tehrani S, Mobarrez F, **Antovic A,** Wallen NH, Lins P-E, Adamson U, Jörneskog G. Atorvastatin has antithrombotic effects in patients with type 1 diabetes and dyslipidemia. Thromb Res 2010, 126: 225-31. PMID: 20637495

http://www.ncbi.nlm.nih.gov/pubmed/20637495

6) Westerlund E, Antovic A, Hovatta O, Eberg KP, Blombäck M, Wallén H, Henriksson P. Changes in Von Willebrand factor and ADAMTS13 during in vitro fertilization. Blood Coag Fibrinolys, 2011; 22:127-31. PMID: 21192251

http://www.ncbi.nlm.nih.gov/pubmed/21192251

7) Mobarrez F, He S, Bröijersen A, Wiklund B, **Antovic A**, Antovic J, Egberg N, Jörneskog G, Wallén H. Atorvastatin reduces thrombin generation and expression of tissue factor, P-selectin and GPIIIa on platelet-derived microparticles in patients with peripheral arterial occlusive disease. Thromb Haemost. 2011; 106:344-52. PMID: 21614411

http://www.ncbi.nlm.nih.gov/pubmed/21614411

8) Mikovic D, Woodhams B, Holmström M, Elezovic I, **Antovic A**, Mobarrez F, Elfvinge P, Antovic JP. On Demand but not Prophylactic Treatment with FVIII concentrate increase Thrombin Activatable Fibrinolysis Inhibitor (TAFI) Activation in HaemophiliaA Patients. Int J Lab Hem 2012; 34:35-40. PMID: 21707936

http://www.ncbi.nlm.nih.gov/pubmed/21707936

9) Westerlund E, Henriksson P, Wallén NH, Hovatta O, Rodriguez Wallberg K, **Antovic A**. Detection of a procoagulable state during controlled ovarian hyperstimulation for in vitro fertilization with global assays of haemostasis. Thromb Res 2012; 130:649-53. PMID: 22154245

http://www.ncbi.nlm.nih.gov/pubmed/22154245

10) Tehrani S, **Antovic A,** Mobarrez F, Mageed K, Lins PE, Adamson U, Wallén NH, Jörneskog. High dose aspirin is required to increase plasma fibrin network permeability in patients with type 1 diabetes. Diabetes Care 2012; 35:404-8. PMID:22148098

http://www.ncbi.nlm.nih.gov/pubmed/22148098

11) Vikerfors A, Mobarrez F, Bremme K, Holmström M, Ågren A, Eelde A, Bruzelius M, **Antovic A,** Wallén H, Svenungsson E. Studies of microparticles in patients with the antiphospholipid syndrome (APS). Lupus 2012; 21:802-5. PMID: 22635239

http://www.ncbi.nlm.nih.gov/pubmed/22635239

12) Antovic JP, Mikovic D, Elezovic I, Holmström M, Elvfinge P, Soutari N, **Antovic A.** Two global haemostatic assays as additional tools to monitor treatment in cases of hemophilia A. Thromb Haemost 2012; 108:21-31. PMID: 22534727

http://www.ncbi.nlm.nih.gov/pubmed/22534727

13) Mobarrez F, Mikovic D, **Antovic A,** Antovic JP. Is a decrease of microparticles related to improvement of hemostasis after FVIII injection in hemophilia A patients treated on demand? J Thromb Haemost 2013; 11:697-703. PMID: 23231463

http://www.ncbi.nlm.nih.gov/pubmed/23231463

14) **Antovic A**, Mikovic D, Elezovic I, Zabczyk M, Hutenby K, Antovic JP. Improvement of fibrin clot structure after FVIII injection in hemophilia A patients treated on demand. Thromb Haemost, 2014; 111:651-6. PMID: 24258360

http://www.ncbi.nlm.nih.gov/pubmed/24258360

15) Vikerfors A, Svenungsson E, Agren A, Mobarrez F, Bremme K, Holmström M, Eelde A, Bruzelius M, Elgue G, Wallén H, **Antovic A**. Studies of fibrin formation and fibrinolytic function in patients with the antiphospholipid syndrome. Thromb Res 2014; 133:936-4. PMID: 24630645

http://www.ncbi.nlm.nih.gov/pubmed/24630645

16) Tehrani S, Jörneskog G, Wallen NH, Elgue G, Majeed K, Henriksson P, Ågren A, Adamson U, Lins P-E, **Antovic A**. Fibrin clot properties and hemostatic function in men and women with type 1 diabetes. Thromb Haemost 2014; Oct 16; 113(2). PMID: 25318636

http://www.ncbi.nlm.nih.gov/pubmed/25318636

17) Vucelic D, Jesic R, Jovicic S, Zivotic M, Grubor N, Trajkovic G, Canic I, Elezovic I, **Antovic A.** Comparison of standard fibrinogen measurement methods with fibrin clot firmness assessed by thromboelastometry in patients with cirrhosis. Thromb Res 2015 135(6):1124-30. PMID:25900310

http://www.ncbi.nlm.nih.gov/pubmed/25900310

18) Mobarrez F, Abraham-Nordling M, Aguilera Gatica K, Friberg I, **Antovic A,** Pisetsky D, Jörneskog G, Wallen H. The expression of microvesicles in the blood of patients with Graves's disease and its relationship to treatment. Clin Endocrinology, 2016; 84:729-35. PMID: 26252432

http://www.ncbi.nlm.nih.gov/pubmed/26252432

19) Grosso G, Vikerfors A, Woodhams B, Adam M, Bremme K, Agren A, Elde A, Bruzelius M, Svenungsson E, **Antovic A.** Thrombin activatable fibrinolysis inhibitor (TAFI) - A possible link between coagulation and complement activation in the antiphospholipid syndrome (APS). Thromb Res 2017; 158:168-173. PMID:28669410

https://www.ncbi.nlm.nih.gov/pubmed/28669410

20) **Antovic A**, Norberg EM, Berndtsson M, Rasmuson A, Mamström RE, Skeppholm M, Antovic J. Effects of direct oral anticoagulants on lupus anticoagulant assays in a real-life setting. Thromb Hemost 2017; 117(9):1700-1704. PMID:28640321

https://www.ncbi.nlm.nih.gov/pubmed/28640321

21) **Antovic A**, Notarnicola A, Svensson J, Lundberg I, Holmqvist M. Venous thromboembolic events in idiopathic inflammatory myopathy - occurrence and relation to disease onset. Arthritis Care Res 2018; Mar 26. doi: 10.1002/acr.23560. [Epub ahead of print]. PMID:29579357

https://www.ncbi.nlm.nih.gov/pubmed/29579357

2.3 The ten most-cited publications

1. He S, **Antovic A**, Blomback M. A simple and rapid laboratory method for determination of haemostasis potential in plasma II. Modifications for use in routine laboratories and research work. THROMBOSIS RESEARCH 2001 103; 5 355-361. *JIF(2017)* 2.779.

Times cited 86.

2. Mobarrez F, He S, Broijersen A, Wiklund B, **Antovic A,** Antovic J, Egberg N, Jorneskog G, Wallen H. Atorvastatin reduces thrombin generation and expression of tissue factor, P-selectin and GPIIa on platelet-derived microparticles in patients with peripheral arterial occlusive disease. THROMBOSIS AND HAEMOSTASIS 2011 106: 2 344-352. *JIF(2017)* 4.95.

Times cited 49.

3. Tehrani S, Mobarrez F, **Antovic A,** Santesson P, Lins PE, Adamson U, Henriksson P, Wallen NH, Jorneskog G. Atorvastatin has antithrombotic effects in patients with type 1 diabetes and dyslipidemia. THROMBOSIS RESEARCH 2010 126;3 E225-E231. *JIF(2017)* 2.779.

Times cited 37.

4. Rooth E, Wallen H, **Antovic A,** von Arbin M, Kaponides G, Wahlgren N, Blomback M, Antovic J. Thrombin activatable fibrinolysis inhibitor and its relationship to fibrinolysis and inflammation during the acute and convalescent phase of ischemic stroke. BLOOD COAGULATION & FIBRINOLYSIS 2007 18; 4 365-370. *JIF(2017)* 1.202.

Times cited 34.

5. He S, Cao H, **Antovic A,** Blomback M. Modifications of flow measurement to determine fibrin gel permeability and the preliminary use in research and clinical materials. BLOOD COAGULATION & FIBRINOLYSIS 2005 16: 1 61-67. *JIF(2017)* 1.202.

Times cited 31.

6. **Antovic A,** Perneby C, Ekman GJ, Wallen HN, Hjemdahl P, Blomback M, He S. Marked increase of fibrin gel permeability with very low dose ASA treatment. THROMBOSIS RESEARCH 2005 116:6 509-517. *JIF(2017)* 2.779.

Times cited 28.

7. Vedin J, **Antovic A,** Eriesson A, Vaage J. Hemostasis in off-pump compared to on-pump coronary artery bypass grafting: A prospective, randomized study. ANNALS OF THORACIC SURGERY 2005 80: 2 586-593. *JIF(2017)* 3.78.

Times cited 27.

8. **Antovic A.** The Overall Hemostasis Potential: A Laboratory Tool for the Investigation of Global Hemostasis. SEMINARS IN THROMBOSIS AND HEMOSTASIS 2010 36; 772-779. *JIF(2017)* 3.345.

Times cited 25.

9. Antovic JP, Hamad RR, **Antovic A,** Blomback M, Bremme K. Does thrombin activatable fibrinolysis inhibitor (TAFI) contribute to impairment of fibrinolysis in

patients with preeclampsia and/or intrauterine fetal growth retardation? THROMBOSIS AND HAEMOSTASIS 2002 88: 4 644-647. *JIF(2017)* 4.95.

Times cited 24.

10. Antovic JP, Yngen M, Ostenson CG, **Antovic A**, Wallen HN, Jorneskog G, Blomback M. Thrombin activatable fibrinolysis inhibitor and hemostatic changes in patients with type I diabetes mellitus with and without microvascular complications. BLOOD COAGULATION & FIBRINOLYSIS 2003 14: 6 551-556. *JIF(2017)* 1.202.

Times cited 23.

2.4 The ten most important publications

1) **Antovic A**, Bremme K, Svenungsson E. Obstetric antiphospholipid syndrome. **Review.** Lupus Science Med. 2018 Sep 25;5(1):e000197. PMID:30364418

   https://www.ncbi.nlm.nih.gov/pubmed/30364418

2) **Antovic A**, Notarnicola A, Svensson J, Lundberg I, Holmqvist M. Venous thromboembolic events in idiopathic inflammatory myopathy - occurrence and relation to disease onset. Arthritis Care Res 2018; Mar 26. doi: 10.1002/acr.23560. [Epub ahead of print]. PMID:29579357

   https://www.ncbi.nlm.nih.gov/pubmed/29579357

3) Grosso G, Vikerfors A, Woodhams B, Adam M, Bremme K, Agren A, Elde A, Bruzelius M, Svenungsson E, **Antovic A.** Thrombin activatable fibrinolysis inhibitor (TAFI) - A possible link between coagulation and complement activation in the antiphospholipid syndrome (APS). Thromb Res 2017; 158:168-173. PMID:28669410

   https://www.ncbi.nlm.nih.gov/pubmed/28669410

4) **Antovic A**, Norberg EM, Berndtsson M, Rasmuson A, Mamström RE, Skeppholm M, Antovic J. Effects of direct oral anticoagulants on lupus anticoagulant assays in a real-life setting. Thromb Hemost 2017; 117(9):1700-1704. PMID:28640321

   https://www.ncbi.nlm.nih.gov/pubmed/28640321

5) **Antovic A**, Mikovic D, Elezovic I, Zabczyk M, Hutenby K, Antovic JP. Improvement of fibrin clot structure after FVIII injection in hemophilia A patients treated on demand. Thromb Haemost, 2014; 111:651-6. PMID: 24258360

   http://www.ncbi.nlm.nih.gov/pubmed/24258360

6) Vikerfors A, Svenungsson E, Agren A, Mobarrez F, Bremme K, Holmström M, Eelde A, Bruzelius M, Elgue G, Wallén H, **Antovic A.** Studies of fibrin formation and fibrinolytic function in patients with the antiphospholipid syndrome. Thromb Res 2014; 133:936-4. PMID: 24630645

   http://www.ncbi.nlm.nih.gov/pubmed/24630645

7) Tehrani S, Jörneskog G, Wallen NH, Elgue G, Majeed K, Henriksson P, Ågren A, Adamson U, Lins P-E, **Antovic A**. Fibrin clot properties and hemostatic function in men and women with type 1 diabetes. Thromb Haemost 2014; Oct 16; 113(2). PMID: 25318636

   http://www.ncbi.nlm.nih.gov/pubmed/25318636

8) Westerlund E, Henriksson P, Wallén NH, Hovatta O, Rodriguez Wallberg K, **Antovic A**. Detection of a procoagulable state during controlled ovarian hyperstimulation for in vitro fertilization with global assays of haemostasis. Thromb Res 2012; 130:649-53. PMID: 22154245

http://www.ncbi.nlm.nih.gov/pubmed/22154245

9) Tehrani S, **Antovic A,** Mobarrez F, Mageed K, Lins PE, Adamson U, Wallén NH, Jörneskog. High dose aspirin is required to increase plasma fibrin network permeability in patients with type 1 diabetes. Diabetes Care 2012; 35:404-8. PMID:22148098

http://www.ncbi.nlm.nih.gov/pubmed/22148098

10) Vucelic D, Jesic R, Jovicic S, Zivotic M, Grubor N, Trajkovic G, Canic I, Elezovic I, **Antovic A.** Comparison of standard fibrinogen measurement methods with fibrin clot firmness assessed by thromboelastometry in patients with cirrhosis. Thromb Res 2015; 135(6):1124-30.

http://www.ncbi.nlm.nih.gov/pubmed/25900310

2.5 List of general articles and book chapters

List of review articles

1. **Antovic A**, Bremme K, Svenungsson E. Obstetric antiphospholipid syndrome. **Review.** Lupus Science Med. 2018 Sep 25;5(1):e000197. PMID:30364418 https://www.ncbi.nlm.nih.gov/pubmed/30364418
2. **Antovic A**. Screening haemostasis – looking for global assays: The Overall Haemostasis Potential (OHP) method – possible tool for laboratory investigation of global haemostasis in hypo- and hypercoagulable conditions. **Review.** Curr Vasc Pharmacol 2008; 6:173-85. PMID: 18673157

   http://www.ncbi.nlm.nih.gov/pubmed/18673157
3. **Antovic A.** The Overall Haemostasis Potential (OHP): a laboratory tool for the investigation of global haemostasis. **Review.** Semin Thromb Hemost, 2010; 36:772-9. PMID: 20978998

   http://www.ncbi.nlm.nih.gov/pubmed/20978998

Book chapters:

Antovic A, Svenungsson E. **The book chapter entitled**: ''Antiphospholipid syndrome'' in the book ''Reumatologi'', by Lars Klareskog, Tore Saxne, Anna Rudin and Lars Rönnblom the 3rd Edition, published 2017.

Vižintin-Cuderman T, Božič-Mijovski M, **Antovic A**, Peternel P, Kozak M and Stegnar M. **The book chapter entitled**: "Association of Haemostasis Activation Markers with Thrombophilia and Venous Thromboembolism" in the e-book "Thrombophilia", ISBN 978-953-307-872-4, published 2011.

2.6 List of all other scientific works

Antovic A. Vikerfors A, Svenungsson E. Antifosfolipidantikroppar, viktiga, men ofta förbisedda riskfaktorer för kärlskador - inom och utom reumatologin. Reuma Bulletinen Vetenskap (Svensk Reumatologisk Förenings Tidskrift) Nr 6/2014.

Antovic A. Effekter av direkta orala antikoagulantia på analyser av lupusantikoagulans. BestPractice Reumatologi Febr 2018.

3 INTERNATIONAL SCIENTIFIC CONGRESSES

3.1 Invited speaker or chair

1. Chair at the Nordic Coagulation Meeting, Stockholm, Sweden, September 5-7, 2018 on session: Global hemostatic assays.
2. Invited speaker on the Congress of the Association of physiatrists of Montenegro, Institute Simo Milosevic Igalo and Clinical Center of Montenegro 18-20 October 2018, on the topic: The future of physical and rehabilitation medicine.
3. Invited speaker on the Serbian National Congress of Rheumatology, Vrnjacka banja, Serbia, September 12-15, 2018, on the topic: Clinical and laboratory markers of ANCA-associated vasculitis.
4. Invited speaker on the Equalis meeting in Stockholm, Sweden 15-16 February 2017, on the topic Clinical manifestations in antiphospholipid syndrome.
5. Invited speaker on the Serbian National Congress of Rheumatology, Kraujevac, Serbia, September 22-25, 2017, on the topic: Antiphospholipid syndrome.
6. Invited speaker on the Serbian National Congress of Rheumatology, Kopaonik, Serbia, September 20-22, 2016, on the topic: Coagulation disturbances in systemic rheumatic diseases.
7. Invited speaker on the Scandinavian Congress of Rheumatology, Stockholm, Sweden, September 20-23 2014 on the topic: Thrombosis and bleeding in rheumatic diseases What`s up?
8. Invited speaker and chairman at the meeting Thrombosis and autoimmunity, 23rd October 2014, Stockholm, Sweden on the topic: Coagulation and inflammation.
9. Invited speaker on the Nordic Coagulation Meeting, Visby, Sweden, September 10-12, 2014 on the topic: Hemostatic disturbances in antiphospholipid syndrome (APS) - can we find a link with inflammation?
10. Invited speaker on the International Meeting of Danubian League against Thrombosis and Haemorrhagic Disorders, Hradec Králové, Czech Republic, May 22-25, 2013 on the topic: Coagulation disturbances in patients with antiphospholipid syndrome (APS).
11. Invited speaker on the International Meeting of Danubian League against Thrombosis and Haemorrhagic Disorders May 14-16, 2009, Belgrade, Serbia on the topic: Factors influencing fibrin structure and function. Relevance to clinical disease.

12. Chairing the session: Thrombotic disorders. Arterial disease mechanisms at XXII ISTH Congress, Boston July 11-16, 2009.

3.2 Oral presentations of own accepted abstracts

1. **Antovic A**, Kostic M, Mobarrez F, Vojinovic J, Gunnarson I. Microparticles as potential biomarkers of disease activity in anti-neutrophila cytoplasmic antibody – associated vasculitis. Oral presentation at Annual European Congress of Rheumatology EULAR 2018, Amsterdam, Netherlands, 13-16 June 2018.
2. **Antovic A**. Effects of new oral (direct) oral anticoagulants on lupus anticoagulant assay. Oral presentation at XXV ISTH Congress Toronto June 20-25, 2015.
3. **Antovic A**, Vikerfors A, Svenungsson E. Thrombin activatable fibrinolysis inhibitor - TAFI as a possible link between coagulation and complement activation in patients with the antiphospholipid syndrome. Oral presentation at 6th International Symposium Women Health Issues in Thrombosis and Hemostasis, Berlin, February 12-15, 2015.
4. **Antovic A**, Mikovic D, Elezovic I, Antovic J. Improvement of fibrin clot structure after FVIII injection in hemophilia A patients treated on demand. Oral presentation at XXIV ISTH Congress Amsterdam July 1-5, 2013.
5. **Antovic A**, Elgue G, Majeed K, Agren A, Henriksson P, Lins, P-E, Adamson U, Wallen NH, Jörneskog G. Oral presentation at 5th International Symposium Women Health Issues in Thrombosis and Hemostasis, Vienna, February 1-3, 2013.
6. **Antovic A**, Elgue G, Majeed K,Agren A, Henriksson P, Lins, P-E, Adamson U, Wallen NH, Jörneskog G. Does a tight fibrin clot in premenopausal women with type 1 diabetes explain the lack of gender difference in cardiovascular disease? Oral presentation at 22nd International Congress on Thrombosis, Nice October 6-8, 2012
7. **Antovic A**, Mobarrez F, Tehrani S, Lins RP-E, Adamson U, Wallen NH, Jörneskog G. Glycaemic Control is of Major Importance for Fibrin Clot Structure in Type 1 Diabetes. Oral presentation at XXII ISTH Congress, Boston July 11-16, 2009.
8. **Antovic A**. Haemostatic disturbances in women undergoing in vitro fertilization (IVF). Oral presentation at the 54th Annual meeting of the Scientific and Standardization Committee of the ISTH, July 2-5, 2008. Vienna, Austria.
9. **Antovic A**, Blombäck M, He S. New overall haemostatic balance method in different conditions with haemostatic disturbances. Oral presentation at the International Symposium on Women's Health Issues in Thrombosis and Haemosatsis, Budapest Hungary 2005, February 4-6.
10. **Antovic A**. Global haemostatic assays presented in the literature. Oral presentation at Subcommittee for Women's Coagulation Issues of the Scientific Standardization Committees of the International Society for Thrombosis and Haemosatsis, Venice, Italy 2004, June 17-19.

11. **Antovic A,** Blomback M, He S. New overall haemostatic balance method in different conditions with haemostatic disturbances. Oral presentation at Nordic Coagulation Meeting, 2004 Stockholm, Sweden.
12. **Antovic A,** Blombäck M. New overall haemostatic balance method in different conditions with haemostatic disturbances. Oral presentation at the International Haematological Days, Nis, Serbia, 2004, October 27-30.
13. **Antovic A,** Petrini P, Blombäck M, Shu He. Determination of Overall Haemostasis Potential in different coagulation factors - deficient plasma and in plasma samples from patients with haemophila A and B. Oral presentation XIX ISTH Congress. Birmingham 2003.

4 RESEARCH FUNDING OBTAINED IN THE PAST FIVE YEARS

4.1 External research funding obtained in international or national competition as *principal applicant*

- 150 000 SEK from Gustav the 5th 80-years foundation 2018 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 100 000 SEK from Reumatikerförbundet 2018 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 75 000 SEK from Reumatikerförbundet 2017 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 75 000 SEK from Reumatikerförbundet 2016 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 100 000 SEK from Swedish Society of Medicine, 2014 for project "The cross-talk between hemostasis and inflammation in patients with antiphospholipid syndrome".

- 23 000 SEK from Karolinska Institutet, 2014 for project "The cross-talk between hemostasis and inflammation in patients with antiphospholipid syndrome".

- 398 800 SEK from Swedish Society of Medicine, 2013 for project "The cross-talk between hemostasis and inflammation in patients with antiphospholipid syndrome".

- 27 000 SEK from Karolinska Institutet, 2013 for project "The cross-talk between hemostasis and inflammation in patients with antiphospholipid syndrome".

4.2 External research funding obtained in international or national competition as *co-applicant*

2014: Vetenskapsrådet: Vascular disease in systemic autoimmunity - Dissecting the characteristics of high risk sub-phenotypes, principal investigator Prof. Elisabet Svenungsson.

4.3 Significant other research funding received (donation, grant in local competition – e.g. ALF project) as *principal applicant*

- 400 000 SEK ALF project for 2018 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 700 000 SEK ALF project for 2019 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 700 000 SEK ALF project for 2020 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

- 400 000 SEK ALF project for 2021 for project "Clinical and laboratory predictors of venous thromboembolism (VTE) in patients with systemic inflammatory diseases".

4.4 Significant other research funding received (donation, grant in local competition – e.g. ALF project) as *co-applicant*

-

5 SCIENTIFIC COLLABORATIONS

2017: We have joined the international collaboration initiated by Prof. Sergey Moiseev at the First Moscow State Medical University. This initiative includes cohorts of patients with ANCA-associated vasculitis (AAV) from France, Czech Republic, Ireland, China and Japan. The collaboration will also include some AAV-cohorts from USA. The meta-analysis of the data may result in the international recommendations for VTE prevention and treatment in AAV patients.
2016-2021: Obtained EU-Erasmus + exchange program grant for teacher- and PhD students exchange between KI and 3 Universities in Serbia (Belgrade, Kragujevac and Nis).
Until now 6 PhD students from Universities in Nis, Belgrade and Kragujevac, Serbia, did parts of their research projects at KI, Dept. of Medicine, Division of Rheumatology (6 months each). Program continues until 2021.

6 SUPERVISION OF GRADUATE STUDENTS

6.1 PhD candidates supervised up to the defence of the candidate's doctoral thesis, with the applicant serving as *main supervisor*

-

6.2 PhD candidates supervised up to the defence of the candidate's doctoral thesis, with the applicant serving as *co-supervisor*

1. Eli Westerlund, thesis May 2013, title: Effects of in vitro fertilization on hemostasis and the relationship between infertility and cardiovascular disease. KIDS.

2. Sara Tehrani, thesis 2014-01-10, title: Studies on haemostasis and microvascular function in patients with type 1 diabetes: effects of treatment with statin and aspirin. KIDS.

3. Anna Vikerfors, thesis 2015-02-24, title: Antifosfolipidsyndrom (APS): clinical, serological and genetic studies. KI, Dept. of Medicine Solna,

6.3 Students supervised up to their licentiate degree, with the applicant serving as *main supervisor*

-

6.4 Students supervised up to their licentiate degree, with the applicant serving as *co-supervisor*

-

6.5 Ongoing supervision of a PhD candidate, with the applicant serving as *main supervisor*

1. Marija Ratkovic Jankovic, University of Nis, Serbia, Medical Faculty. Project: Markers of inflammation in renal tissue after active treatment of lupus nephritis.

2. Milena Kostic, University of Nis, Serbia, Medical Faculty. Project: Neutrophil microparticles in ANCA-associated vasculitis.

6.6 Ongoing supervision of a PhD candidate, with the applicant serving as *co-supervisor*

1. Maria Farm, KI, Dept. of Molecular Medicine and Surgery. Registered April 2014, project: Evaluation of new global hemostatic analysis in venous thromboembolism and thrombophilia. Half-time September 2018. Thesis May 2020.

2. Giorgia Grosso, KI, Dept. of medicine Solna, Rheumatology Unit. Registered December 2015, project Thrombotic and Cardiac disease in the Antiphospholipid Syndrome (APS). Planed half-time March 2019. Thesis September 2020.

6.7 Postdoc supervision

6.8 Supervision of other researchers who have defended a thesis

-

6.9 Ongoing careers of holders of earlier PhDs and of postdocs

-

7 THESIS EVALUATION

7.1 Serving as thesis opponent

- 2010: Opponent on a PhD thesis "Evaluation of the overall haemostatic potential assay for the diagnosis and management of hypercoagulable states" by Jennifer Leigh Curnow, University of Sydney, Australia.

- 2008: Opponent on a PhD thesis "Studies on subfractions of fibrinogen. With special emphasis on fibrinogen quantification, viscosity and inflammation", by Dr Torstein Jensen, University of Oslo, Norway.

7.2 Serving as a member of a thesis examination committee

2018: Betygsnämd ledamot för avhandling: "When systemic lupus erythematosus (SLE) involves pain: occurence and impact on daily life", Eva Waldheim, NVS, H1, Sektionen för omvårdnad, Karolinska Institutet.

2017: Member of examination committee: "Application of Swedish quality registry data for use in health economic assessments of chronic diseases", Ingrid Lekander, MMC/LIME vid Karolinska Institutet.

7.3 External thesis reviewer

-

8 EVALUATION OF OTHERS' WORK

8.1 Serving as reviewer of candidates proposed for academic positions

-

8.2 Serving as reviewer for international evaluations

-

8.3 Evaluator of research applications in international competition

1. December 2012: National Children's Research Centre, Ireland application by Prof. Naomi McCallion titled "Fetal, neonatal and maternal diagnostic and management implications of enhanced thrombin generation in plasma of mothers with early onset preeclampsia".

2. October 2013: The National Research Foundation (NRF) South Africa, application by Prof M Pieters, (North-West University) titled "Haemostatic CVD risk factors in Africans- a 10 year prospective study."

8.4 Evaluator of research applications in national competition

-

8.5 Evaluator of major research grant applications in local competition

-

8.6 Editor of scientific journals

-

8.8 Member of an editorial board

-

8.8 Referee for scientific journals

- Thrombosis Research
- Thrombosis & Haemostasis
- Journal of Thrombosis & Haemostasis
- British Journal of Haematology

8.8 Reviewer or advisor for other scientific bodies

-

8.9 Other relevant evaluation assignments

-

9 INTERNATIONAL VISITING RESEARCH FELLOWSHIPS

-

10 SCIENTIFIC DISTINCTIONS

2009: Annual Award from Karolinska Institutet Danderyd Hospital for the best research project in year 2009.

2003: Young Investigator Award by the International Society on Thrombosis and Haemostasis (ISTH)

11 OTHER SCIENTIFIC MERITS

-

12 RESEARCH PLAN

I have performed research in the field of haemostasis since 2000. My research activities can be divided into three different phases:

1) The PhD studies,

2) The Post doc activities (1 year in Slovenia and 2 years at Danderyd hospital, KIDS)

3) Present research activities and plans for the future work

1) The main research subject of my PhD thesis was development of a new global haemostatic assay called Overall Haemostasis Potential (OHP) in plasma.

The main aim with this work was to provide new, global and rapid haemostatic method which would be useful for screening of both hyper- and hypocoagulable disorders. Respectively, the OHP assay was evaluated in connection with hypercoagulation in normal pregnancy, preeclampsia, coronary heart disease, diabetes, stroke, vascular surgery, as well as in patients with previous thromboembolim related to the presence of FV Leiden mutation. Promising results were obtained regarding the application of the OHP assay in detecting deficiency of coagulation factors. Monitoring anticoagulant treatment is one of possible application of this method as well as monitoring the effects of by-passing agents such as FVIIa.

Another part of my research work during the PhD studies was investigation of fibrin clot structure using the permeability assay and microscopy imaging. The mechanism of acetylsalicylic acid – aspirin action on the fibrin clot permeability was studied in healthy subjects (as a part of my PhD project, ref. 4 and 6 in the thesis) as well as in patients with type 1 diabetes mellitus (ref 10 above, original publications after PhD).

In the evaluation of my research activities for award from Karolinska Institutet Danderyd Hospital as the best researcher in year 2009 is written: "*På ett föredömligt sätt har Aleksandra Antovic utvecklat nya metoder att studera hemostasmekanismer som hon utnyttjar för att i kliniska studier undersöka patienter med ökad risk för aterosklerotiska komplikationer. Detta kan leda till ökad kunskap och förbättrad behandling hos stora patientgrupper.*"

2) Shortly after disputation I started to work as a Postdoc at the Dept of Angiology, Clinical Centre Ljubljana, Slovenia in the group of Professor Mojca Stegnar with the emphasis on establishment and evaluation of the OHP assay in their research laboratory. Investigations were performed in patients with hypercoagulable disorders such as young patients with a previous ischemic stroke (ref no 2 above, original publications after PhD) and patients with first deep venous thrombosis in lower limbs. The slightly modified OHP assay, employing tissue factor (TF) as initiator of

coagulation, was used to monitor in vitro effects of novel type of antithrombotic compounds.

After obtaining the stipend from Karolinska Institutet and David & Astrid Hagelèns Foundation I have continued my Postdoctoral work at the Department of clinical sciences, KIDS. During that time and during the research block of my general-research internship, I have worked on a project investigating hemostasis in patients with diabetes mellitus type 1 in relation to gender with focus on glycaemic control, coagulation, global haemostatic parameters and fibrin clot formation, as well as effects of aspirin and statins on these haemostatic variables (ref. 4, 5, 7, 10, above, original publications after PhD). This project was granted by several foundations during the period from 2006 to 2011 (as described above).

I became a co-supervisor to a PhD student Sara Tehrani at KIDS working on the same project and the final manuscript of this work was recently published (ref. 16, above, original publications after PhD) after thesis defence 2014-01-10.

In addition, during my Postdoc period as well as during my Research-general internship I have been working with the following projects/activities:

I have started co-supervising two PhD students at Karolinska Institutet (KIDS). One of them, dr Eli Westerlund defended thesis in May 2013 investigating haemostatic disturbances in women undergoing in vitro fertilization (IVF). The effects of IVF on single coagulation factors and global haemostatic parameters were studied in details (ref 6 and 9 above, original publications after PhD). This project was granted by Swedish Society of Medicine and Tore Nilssons foundation between 2009 and 2011 (as described above).

The studies of haemostatic disturbances in patients with haemophilia A and comparing different global haemostatic assays in monitoring FVIII concentrate treatment in these patients in relation to the levels of microparticles and fibrin clot structure are also of high importance for my work, (ref. 12, 13, 14 above, original publications after PhD).

3) The co-supervision of the PhD student dr Anna Vikerfors from the KI, Dept of Medicine Solna and Rheumatology clinic, Karolinska University Hospital has opened up the possibilities to investigate haemostatic parameters in patients with systemic autoimmune diseases like systemic lupus (SLE) and antiphospholipid syndrome (APS). There are ongoing studies on possible pathophysiological mechanisms underlying thrombosis development in these patients with focus on microparticles (ref. 11, above, original publications after PhD), fibrin structure and fibrinolysis (ref 15, original manuscripts after PhD), as well as complement activation (unpublished data, presented at EULAR meeting in Amsterdam 2018).

Research plan: Investigation of possible links between coagulation and inflammation in autoimmune inflammatory diseases is a primary goal in my future research at the Rheumatology Unit, Dept. of Medicine, Solna, KI. The project is entitled: "Predictors of venous thromboembolism (VTE) in patients with systemic autoimmune diseases".

VTE includes deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT is a common thrombotic vascular condition affecting about 1/1000 people per year, while PE is the third most common "cardiovascular disease",

following myocardial infarction and stroke. Around 4000 PE are treated in Sweden each year, being a cause of death in around 1000 patients.

The data on VTE in systemic autoimmune diseases had been scarce in the literature, but in the past few years, multiple studies suggesting an association between systemic autoimmune diseases and VTE have been emerging. It is becoming more recognized that active inflammation characterizing systemic autoimmune rheumatic diseases increases coagulability and leads to thrombosis. Inflammation-induced VTE is considered to be a feature of systemic autoimmune diseases such as Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). More recently accumulating data have demonstrated a significant increase in thromboembolic events both in ANCA-associated vasculitis (AAV) and large-vessel vasculitis (LVV), especially during active disease. Furthermore, vascular involvement is regarded a major contributing factor to mortality in patients with idiopathic inflammatory myopathies (IIM) including polymyositis (PM) and dermatomyositis (DM). These findings have important consequences in terms of management and treatment; perhaps one might speculate that an aggressive anti-inflammatory treatment during active phases could remodel vascular involvement especially in early stages of these diseases. However, despite the mechanistic links between rheumatologic diseases and VTEs, these highly inflammatory conditions may be under-recognized as risk factors for hypercoagulability.

This project includes studies of VTE in consecutive cohorts of patients with SLE, systemic sclerosis, AAV and idiopathic inflammatory myopathies (IIM) followed at the Rheumatology clinic Karolinska University Hospital:

I. SLE is a chronic autoimmune disease, characterized by the production of autoantibodies, which together with complement factors form immune complexes, initiating systemic inflammation in affected organs with different grade of organ damage as a consequence. A very heterogeneous presentation and a remarkable female predominance (90%) are typical features of SLE. According to recent cross-sectional Swedish study, around 16% of SLE-patients are affected by VTE. There is a well-known association between the presence of antiphospholipid antibodies in SLE and both venous and arterial thrombosis, but SLE per se exerts prothrombotic effect based on the innate hypercoagulability nature of this inflammatory disease.

The female predominance in systemic sclerosis (SSc) is 80% and many, but not all, symptoms and autoantibodies overlap with SLE. The main causes of mortality in SSc are heart and lung manifestations. A vascular hyperreactivity/spasm, which with time develops into permanent vascular damage and impaired blood flow, is characteristic. Microvascular disease is common and well described in SSc, but macro vascular disease and VTE is less well studied.

Patient cohorts: Detailed cross-sectional studies are performed every 10 years on our SLE cohort comprising 480 patients and 320 population controls individually matched in the population registry for age, gender and area of living to the first 320 SLE patients. The 3rd 10-year follow up is initiated at the moment. We now plan to include also SLE patients at the Huddinge site of our clinic, and we hope to reach a total of 700-750 SLE patients, i.e. 70-75% of the approximately 1000 SLE patients in the Stockholm County (according to national registries).

Since 2009 blood samples have been collected from 100 patients with APS and 100 controls have been collected at the Rheumatology clinic, Karolinska University

hospital. During 2015 a new and rigorous inclusion of APS patients and matched controls has started. This inclusion will follow a similar protocol to the ongoing SLE study. Results will thus be comparable between these studies further enhancing our possibilities for subgroup analyses and comparisons.

The cohort of patients with SSc comprising 111 patients and 105 population-based controls have been included between 2006 and 2009 at the Rheumatology clinic, Karolinska University hospital. Detailed follow-up of this cohort is also ongoing.

This part of the project will be performed in collaboration with Prof. Elisabet Svenungsson, consultant physician at the Rheumatology clinic Annica Nordin and PhD student Giorgia Grosso.

II. ANCA-associated vasculitis (AAV) constitutes a group of primary vasculitides associated with the presence of circulating anti-neutrophil cytoplasmic antibodies (ANCA). AAVs comprise granulomatosis with polyangiitis (GPA, previously Wegener's granulomatosis), microscopic polyangiitis (MPA) and Churg–Strauss syndrome (CSS). AAVs are potentially organ- or life-threatening, chronic inflammatory autoimmune diseases characterized by granulomatous inflammation and necrotizing vasculitis predominantly affecting small- to medium-sized blood vessels. The prevalence of AAV is 100-300/million with incidence of 30-40 new cases/million/year. The kidneys are affected in approximately 70% of patients increasing the risk of renal damage which may result in the need for dialysis or kidney transplantation. Between 50-70% patients relapse during the 10-year period, while others have residual disease activity despite ongoing immunosuppressive treatment.

Patient cohort: There is a standardized follow up of patients with AAV at the rheumatology- and nephrology clinic at the Karolinska University hospital since 2008. Patients with diagnosis MPA, GPA and CSS are included in cross-sectional study (`VASKA`). A structured clinical examination has been conducted of all patients with assessment of disease activity (BVAS), chronicity / organ injury Index (VDI), co-morbidity, incidence of arteriosclerosis and heredity conditions and environmental factors such as smoking. To date, approximately 300 patients are enrolled in the study and a large detailed database has been established. Newly diagnosed patients are also followed prospectively (0, 3, 6 months and 2-5 years) with structured follow-up program with regular assessment of disease activity (VASCA-Long). More than 100 patients are included in the longitudinal study.

This part of the project will be performed in collaboration with Assoc. Prof. Iva Gunnarsson, from the Rheumatology clinic and Prof. Annette Brushfeld, Nephrology clinic at the Karolinska University hospital.

III. The idiopathic inflammatory myopathies (IIMs) collectively called myositis, are chronic inflammatory diseases clinically characterized by muscle weakness and muscle fatigue. A typical finding is inflammatory infiltrates in skeletal muscle tissue. Other organs are often involved such a skin, lungs, joints and sometimes the heart. Treatment is based on high doses of glucocorticoids in combination with immunosuppressive drugs e.g. methotrexate or azathioprine. Despite this treatment many patients develop a sustained impairment with low quality of life and they have an increased mortality due to cardiovascular disease, malignancies and lung disease. Recently two register based studies one from Sweden and one from Canada suggest that patients with IIM have an increased risk

VTE. The mechanisms behind the increased risk of thromboembolic events are not fully explored.

Patient cohort: In the rheumatology clinic at Karolinska University hospital we have a standardized follow up of patients with myositis since more than 10 years and we follow the patients with annual evaluation using validated outcome measures for disease activity and damage. In the damage score MYODAM, thromboembolic complications are registered.

Clinical data are available concerning demographic data, disease activity, (IMACS disease activity core set), autoantibody profile, and from time of thromboembolic complication also data regarding hypertension, diabetes and dose of prednisolone, immunosuppressive treatment.

This part of the project will be performed in collaboration with Prof. Ingrid Lundberg, and consultant physicians and PhD student Antonella Notarnicola from the Rheumatology clinic Karolinska University hospital.

Aims of the project:

The **main goal** of these studies is to investigate the incidence of VTE in patients with systemic autoimmune inflammatory diseases as well as clinical and serological characteristics of these high-risk patients in comparison to patients without a history of VTE after the diagnosis.

For this purpose following studies are aimed:

1. The cross-sectional studies to analyze underlying mechanisms behind the development of thrombotic complications in patients with SLE, SSc, AAV and IIM, with the special focus on potential links between coagulation and inflammation in these patients.

2. The prospective studies to evaluate predictive value of different coagulation/fibrinolysis markers in estimating the risk for development of thrombotic complications in prospective cohort studies of SLE, SSc, AAV and IIM patients.

In focus:

The molecular links between inflammation and coagulation in autoimmune diseases have not yet been well characterized. Thrombin-activatable fibrinolysis inhibitor (TAFI), a plasma pro-carboxypeptidase-B, may be of particular interest. TAFI is a component of the coagulation pathway that protects blood clots from fibrinolysis. Active enzyme - TAFIa removes carboxyl-terminal lysine residues from partially degraded fibrin, thus maintaining fibrin clots and having a prothrombotic function. The inflammatory peptides bradykinin, osteopontin and anaphylatoxins C3a and C5a are also substrates for TAFIa. Therefore, by suppressing the activity of these proinflammatory mediators TAFIa may have antinflammatory function. This dual role of TAFIa raises the question: Is a down-regulation of fibrinolysis by TAFI a price which is paid for the beneficial effect of TAFI in decreasing inflammation at the site of vascular injury?

Another important feature in hemostasis activation, which can be of importance for the cross-talk between coagulation and inflammation are microparticles (MPs), the subcellular structures (<1μm) derived from different cell types (mostly platelets and endothelial cells) after activation and/or apoptosis. Increased levels of MPs are also associated with inflammation and complement activation as well as thrombotic manifestations.

The citrate plasma, serum and the whole blood samples will be used for in vitro analysis of different coagulation- and fibrinolysis biomarkers: fibrinogen, fibrin formation with the overall hemostasis potential method, fibrin porosity-structure, von Willebrand factor, thrombin generation in plasma with the endogenous thrombin potential method, clot lysis time, markers of endothelial activation as VCAM, ICAM, endotelin-1, thrombomodulin, thrombin activatable fibrinolysis inhibitor (TAFI) and complement components as C3a and C5a.
Microparticles (MPs) are defined as phospholipid particles <1 μm in size by flow-cytometry. For characterization the cellular origin of MPs they are incubated with monoclonal antibodies, i.e. platelet-derived MPs (CD42a, PMPs), endothelial-derived MPs (CD144/CD62E, EMPs) or leukocyte-derived MPs (CD45, LMPs). Expression of inflammation or coagulation markers can also be measured on MPs such as CD142 (Tissue factor), CD154 (CD40 Ligand) or HMGB1, thrombomodulin or endotelin-1. Additionally, we can measure the amount of nuclear material (DNA/mRNA) inside of MPs by labeling them with the dye SYTO 13.

Analyses of coagulation/fibrinolysis markers will be performed at the research laboratory Dept. for Molecular Medicine and Surgery KI by two BMA included in the project. Microparticles will be analysed at the research laboratory Dept. of Clinical Sciences KI Danderyd Hospital by postdoc F. Mobbarez.

Importance:

Better overview of the incidence and pathogenesis of VTE in patients with systemic autoimmune rheumatic diseases is of a great importance taking into consideration the health- and economic burden of the treatment and follow-up of these complications. Overall objective of the project is to try to identify risk factors and understanding the mechanisms of thrombotic events in patients with systemic autoimmune diseases. The goal is to define the patients at high risk for VTE complications and adjust better treatment strategies. The knowledge and clinical experience from this project should lead to favourable prognosis for individual patients.

KAROLINSKA INSTITUTET
TEACHING PORTFOLIO

1 SUBJECT AREA COMPETENCE AND CURRENT TEACHING ACTIVITY

Clinical rheumatology, at undergraduate level at KI, Medicine course, T4 and T5.

Thrombotic complications and anticoagulant treatment at KI, at undergraduate level, Medicine course, T5 and T6. Teaching includes cathedral lectures, seminars as well as bed-side teaching.

From HT 2015 I will start to work as a clinical amanuens at Rheumatology clinic Karolinska University Hospital Huddinge.

Hemostasis, coagulation and fibrinolysis, laboratory assays in hemostasis at postgraduate level.

2 TEACHING IN THE STUDY PROGRAMME

2.1 Scope/time of teaching

Responsible for education of medical students at the Academic Specialist Center, Center for Rheumatology, Stockholm Health Services.

2.2 Form of instruction

Cathedral lectures, seminars, laboratory instruction and demonstrations, supervision in practice-based instruction such as bed-side instructions for medical students, supervision of individual project assignments.

2.3 Teaching assignments

2017 at present: Responsible for education at the Academic Specialist Center, Center for Rheumatology, Stockholm Health Services.

2015 -2017: amanuens position at Rheumatology clinic Karolinska University Hospital Huddinge.

2.4 Examination and assessment

Organization of courses and meetings:

Organizing the meeting "Thrombosis in autoimmunity" 23rd of October 2014, Karolinska University Hospital, Stockholm, Sweden.

Organizing and being responsible for the assessment of the results at the PhD course No 1709 "Sex hormones and cardiovascular disease. What we know and what we do not know?" KIDS, VT 2009.

2.5 Production of study materials and instructional materials

Book chapters:

1. Antovic A, Svenungsson E. **The book chapter entitled**: "Antiphospholipid syndrome" in the book "Reumatologi", by Lars Klareskog, Tore Saxne, Anna Rudin and Lars Rönnblom the 3rd Edition, published 2017.
2. Vižintin-Cuderman T, Božič-Mijovski M, **Antovic A**, Peternel P, Kozak M and Stegnar M. **The book chapter entitled**: "Association of Haemostasis Activation Markers with Thrombophilia and Venous Thromboembolism" in the e-book "Thrombophilia", ISBN 978-953-307-872-4, published 2011.

2.6 Course evaluation, and evaluation of instruction and study programme

-

2.7 Internationalisation

-

3 TEACHING IN NURSING AND MEDICINE AND FOR HEALTHCARE PRACTITIONERS

3.1 Teaching in nursing and medicine

-

3.2 Teaching for healthcare practitioners

-

4 DEVELOPMENT OF TEACHING SKILLS

4.1 Formal studies in university-level teaching

Courses undertaken at Karolinska Institutet

"Pedagogy for university teachers", VT 2008, **(3 weeks - 4.5 pt)**

"Information Technology in education" HT 2008, **(1 week - 1.5 pt)**

"Feedback in education" HT 2008, **(1 week - 1.5 pt)**

"Course in Supervising PhD students**"** VT 2012

"Course in Good Clinical Practice" Karolinska Trial Aliance VT 2012

4.2 Other teaching activities

5 DEVELOPMENT WORK IN TEACHING/MEDICAL PEDAGOGY

5.1 Pedagogical development work and projects

5.2 Communication and presentations of pedagogical development work

6 TEACHING DISTINCTIONS

2016: Educational award from Department of medicine, Karolinska University Hospital, Huddinge. Motivering: " Docent Aleksandra Antovic har på ett excellent sätt utvecklat och organiserat undervisningen för kursen i klinisk medicin vid reumatologiska kliniken, Karolinska Universitetssjukhuset, Huddinge. Genom god studentkontakt baserat i ett starkt personligt engagemang har Aleksandra Antovic tillfört undervisningen i reumatologi vid kursen i klinisk medicin ett mervärde som uppskattas av såväl studenter som kursledning."

7 OTHER TEACHING MERITS

-

8 CONCRETE EXAMPLES AND REFLECTIONS ON YOUR OWN TEACHING

Pedagogical activities are the key-stone of working in academic environment and a combination of teaching within both research and clinical work under the frame of biomedical studies offers an excellent environment for the development of pedagogical skills and merits.

From the early begging of my undergraduate medical studies (termin 7) I worked as a student teaching assistant at the Biochemistry department, Medical faculty Nis, Serbia. After finishing undergraduate studies, I enrolled master studies at the Biochemistry department, Medical faculty Nis, Serbia combining this with my general internship in order to continue both academic and professional education. After relocation to Sweden, and during PhD studies I have not been engaged in the teaching activities on the undergraduate level due to the language barrier, but in spite of that I was included in the teaching activities in the laboratory, as well as scientific rapports, seminars and journal clubs held in English.

During my Postdoc position at Karolinska Institutet, and after mastering Swedish language I have actively participated in the teaching of undergraduate students during the cathedral lectures and seminars on different undergraduate courses but also in the laboratory for student- research projects. After obtaining general research internship position at Karolinska Institutet Danderyd Hospital, I have continued with cathedral lectures, seminars at the same time as I have participated in the bed-side education of undergraduate students. After obtaining the Swedish medical licence in 2011 I have continued to work as a resident at the Dept of Rheumatology, Karolinska University Hospital where I continued teaching activities on the undergraduate level as well as on the research level. I do believe that those activities will progressively increase in the future.

In the meantime I have had several cathedral lectures on the postgraduate courses and participated in organizing one postgraduate course at KIDS, as mentioned above. My pedagogic merits were internationally recognized since I was the opponent for the PhD thesis at the University of Oslo and the reviewer of the PhD thesis at the University of Sydney, and I have participated in the education of PhD students in my former home city Nis at the Medical Faculty. Finally, I plan to continue my pedagogical activities by supervising PhD students. I have already started this, being a co-supervisor to five PhD students, and hopefully I will become the main supervisor for some PhD student(s) in the near future.

In order to accomplish and improve my teaching I have completed the pedagogic education by accomplishing the obligatory course for supervisors at Karolinska Institutet. I have applied for KID-founding as a main supervisor for a PhD student. In parallel I am responsible for education of medical students at the Academic Specialist-Center, Center for Rheumatology, Stockholm Health Services.

Karolinska Institutet is considered as one of the most prestigious educational centres in the field of biomedicine in Europe and in the world. Therefore, a possibility to teach here is a great honour, but also an extremely demanding task. I hope that my merits and skills, but above all the gratification in work with students, could be promising grounds for my future pedagogic career.

KAROLINSKA INSTITUTET
CLINICAL PORTFOLIO

1 CLINICAL SPECIALIST EXPERTISE AND CURRENT ACTIVITY

2017 – at present: Consultant in Rheumatology at the Academic Specialist Center, Center for Rheumatology, Stockholm Health Services.

20% of employment at the Rheumatology clinic Karolinska University hospital.

2012-2017: Resident at the Rheumatology clinic Karolinska University Hospital Huddinge with the clinical experience with in- and outpatients.

2 CLINICAL EXPERTISE AND FORMAL TRAINING (INCLUDING PUBLIC HEALTH WORK)

2.1 Completed clinical training

•*Faculty of Medicine Nis, Serbia*

Medical Doctor (average mark 9.22 (6.00-10.00)), 1992-1999.

• *Clinical Medical Center Nis, Serbia.*

General Internship 1999-2000.

• *Department of medicine, Danderyd Hospital, Stockholm, Sweden*

September 2008 - February 2009: junior physician

• *Danderyd Hospital, Stockholm, Sweden*

March 2009 – December 2011: General-research internship

•*Karolinska University Hospital, Stockholm, Sweden*

2012-2017: Rheumatology resident at the Rheumatology clinic.

Clinical experience within general internship of inpatient and outpatient care within surgery, internal medicine, psychiatry and primary care.

Clinical experience with in- and outpatients at the Clinic of Rheumatology but also Internal medicine and Cardiology Clinic, Nephrology Clinic, Immunology clinic and Clinic for Infectious Diseases as a part of my speciality education.

Clinical and laboratory experience in diagnosis and treatment of thrombotic disorders (venous thromboembolism, thrombophilia). Monitoring of oral anticoagulant treatment and treatment with standard- and low molecular weight heparin.

2.2 Specialist expertise

Rheumatology

2.3 Clinical positions

2017 – at present: Consultant in Rheumatology at the Academic Specialist Center, Center for Rheumatology, Stockholm Health Services.

20% of employment at the Rheumatology clinic Karolinska University hospital.

2.4 Clinical supervisory positions

2.5 On-call activity

During general internship and during clinical rotations at Internal medicine clinic and Cardiology clinic around 40% of time was aimed for the on-call activities (night duties at the Emergency departments).

3 CLINICAL DEVELOPMENT WORK (INCLUDING PUBLIC HEALTH)

3.1 Efforts resulting in significantly improved clinical care provision

In the evaluation of my research activities for award from Karolinska Institutet Danderyd Hospital as the best researcher in year 2009 is written: *"På ett föredömligt sätt har Aleksandra Antovic utvecklat nya metoder att studera hemostasmekanismer som hon utnyttjar för att i kliniska studier undersöka patienter med ökad risk för aterosklerotiska komplikationer. Detta kan leda till ökad kunskap och förbättrad behandling hos stora patientgrupper."*

These new laboratory methods are now the part of research laboratories both at Danderyd Hospital as well as Karolinska University Hospital. There is an ongoing continuous evaluation of these assays in diagnosis of hemostatic disturbances with a goal to make them useful in routine diagnostics.

3.2 Area of expert knowledge

33. Responsibility for a diagnostic group

3.4 New treatment forms and diagnostics

3.5 Clinical trials

Formal education:

Course in Good Clinical Practice, Karolinska Trial Aliance VT 2012 (certificate enclosed).

Participation in clinical trials:

I actively participated in 2 ongoing clinical trials investigating effects of disease modifying drugs and new anti-inflammatory drugs in patients with rheumatoid arthritis at the Rheumatology clinic Karolinska Hospital. These are C-early and NORDSTAR trials, both fase-4 trials, with Prof. Ronald van Vollenhoven as a main investigator. My contribution in these trials is recruitment of the patients and clinical evaluation of the treatment.

The NORDSTAR trial includes patients with early diagnosed rheumatoid arthritis from all Scandinavian countries, so far 200 patients are included and the plan is to include 600 patients in order to evaluate 4 different treatment regiments for this group of patients.

The C-early trial aimed to evaluate the effect of two different doses of this TNF-alpha inhibitor in patients with early diagnosed RA.

3.6 Care programme and clinical guidelines

May 2014 – at present: Establishing and updating the clinical guidelines for investigation and treatment of patients with antiphospholipid syndrome at Rheumatology clinic Karolinska University Hospital.

3.7 Clinical supervision

3.8 Pharmaceuticals

3.9 Clinical use of results achieved in a specific medical field

3.10 Clinical fellowship

3.11 Preventive work

4 CLINICAL DISTINCTIONS

5 OTHER CLINICAL MERITS

6 DEVELOPMENT PLANS IN HEALTHCARE AND PUBLIC HEALTH

By identifying target groups of specialists involved in diagnostic and treatment of patients with antiphospholipid syndrome (APS) and establishing guidelines for the treatment of this disease I intend to initiate formation of the Centre of excellence at Karolinska University Hospital for the diagnosis and treatment of this complicated disease which requires multidisciplinary approach and sophisticated treatment. The major clinical manifestations of APS are thrombosis, both in arterial and venous blood vessels, as well as pregnancy complications resulting in repeated miscarriages. The socio-economic burden of life-long treatment, laboratory monitoring and prevention of possible complications in patients with APS is the issue which has not been previously discussed in Swedish health system.

The Centre of excellence for APS will engage a broad spectrum of expertise starting with specialists in Clinical Chemistry and Clinical Immunology responsible for laboratory diagnosis of APS. The assays which are available at the moment are rather new, not completely evaluated in clinical praxis and with high intra- and inter-laboratory variability. The standardisation of the diagnostic procedures is one of the primary goals of this project.

Regarding the clinical issues in APS, the multidisciplinary approach is required including professional team with specialists in Rheumatology, Haematology, Coagulation, Gynaecology, Nephrology, Lung medicine, Cardiology, Dermatology, since these patients can have involvement of different organs, in some cases leading to multiple organ failure and requesting treatment at intensive care units.

Moreover, the treatment of APS is challenging, since these patients require a live-long treatment with anticoagulant drugs, combined with immunosuppressive treatment. The monitoring of anticoagulant treatment is obliged and cannot be provided by primary care physicians since APS is complex autoimmune disease, developing unpredictable flairs with increased thrombotic risk during the observational time.

Finally, the gender perspective of APS is of high importance. Around 90% of patients are women in reproductive age. These patients need a careful and highly specialized approach to pregnancy maintenance, with proper anticoagulant and immunosuppressive treatment in order to avoid miscarriages and other pregnancy complications. The advising regarding contraceptive treatment is crucial since the oral contraceptive treatment is not recommended.

Since the New Karolinska University Hospital is aiming to have a high competence profile, the model of multidisciplinary approach is a prerequisite, particularly in complex patient categories such as patients with antiphospholipid syndrome.

KAROLINSKA INSTITUTET
LEADERSHIP, DEVELOPMENT AND COLLABORATION PORTFOLIO

1 CURRENT ACTIVITIES INVOLVING MANAGERIAL RESPONSIBILITY

Together with clinical and academic improvement I have developed skills and knowledge that enables me to engage and lead in complex and rapidly changing environments such as every-day clinic practice as well as research settings. This includes several leading roles which might vary during the same day, interfering with each other and being balanced on the high intellectual level. There are daily situations where I lead a team work at the clinic at the same time having responsibility for education of the medical students and residents from other clinics as well as being responsible for the ongoing projects in the laboratory.

Development of medical leadership has been an essential component of my education and professional work including all ground principles of medicine: the welfare of patients, the education of medical students, and the research. Above all, being a physician brings forth a social responsibility to speak out on health issues which puts a physician in a position of apparent leadership on many aspects of health.

2 TRAINING IN LEADERSHIP, DEVELOPMENT AND COLLABORATION

2.1 Formal education and degrees

March 2015: Completed LUST course (Leadership development for residents at Karolinska University Hospital,

2.2 Completed courses/study programmes

3 EXPERIENCE:

2017 – at present: Responsible for education of medical students at the Academic Specialist Center, Center for rheumatology.

2017 – at present: Member of the FOUU-council at the Academic Specialist Center, Center for rheumatology.

2015- 2017: Clinical amanuens position at Rheumatology clinic Karolinska University Hospital Huddinge.

November 2013: Member of a National Cardiovascular Working group for rheumatologic diseases. Within the activities of this group I was responsible for organization and a part of the scientific comity of the meeting "Thrombosis in autoimmunity" on the 23rd of October 2014.

May 2014: Responsible for establishing and updating the clinical guidelines for investigation and treatment of patients with antiphospholipid syndrome at Rheumatology clinic Karolinska University Hospital.

2011 – 2013: Responsible for education of laboratory personal in establishing different global hemostatic assays at the Dept. of Coagulation Research, Dept. of Molecular Medicine and Surgery, KI.

2007 – 2011: Responsible for the set up and development of the working environment of the research laboratory at the Department of clinical sciences KIDS including systematization of the equipment, the storage and control of chemical reagents and supplies of the laboratory material. I have initiated and actively participated in organization of weekly meetings of the research group. I was also responsible for the continued education of the laboratory stuff regarding the hemostatic assays.

The leading role in research projects became more evident after receiving several independent research grants (as stated in the scientific portfolio) and resulting in several scientific publications with senior authorship.