

CV for Henrik Hjorth-Hansen born Dec 1st 1960

Education and employment:

Secondary school Trondheim Katedralskole	1979
Medical School: Linköping, Sweden	1985
Compulsory internship Elverum County Hospital	1986
and Lavangen kommune (municipality)	1987
Military service (Army Medical Corps)	1987-1988
Dept of Psychiatry, Trondheim University Hospital	1988-1989
Dept of Internal Medicine, Norrköping Sweden	1989-1993
Dept of Internal Medicine Trondheim University Hospital	1993-1994
Research Fellow Inst of Cancer Research and Molecular Biology	1995-1999
Specialist of General internal medicine in Norway and Sweden since	1997
Dept of Hematology, Clinic of Internal Medicine, St Olavs Hospital	2000-2003
Dept of Oncology (Kreftavdelingen) St Olavs Hospital	2003
Postdoctoral periods (altogether 6 months)	2001+2003
Section of Hematology, Dept of Internal Medicine, St Olavs Hospital	2004-now
Specialist in Hematology	Jan 2005
Ass professor II (førsteamanuensis) NTNU (10% position)	2004-2013

Current positions:

Consultant Dept of Hematology, St Olavs Hospital (Trondheim University Hospital) since 2005. Dept head 2017

Prof of Hematology . Faculty of Medicine NTNU; from JUN2013 (20% position). Unit Lead Hematology DEC 2016

Thesis:

Novel cytokines in growth control and bone disease in multiple myeloma 2001 NTNU

Awards:

Best Abstract Nordic Hematology Spring meeting Linköping 2002 (10.000,- SEK)

Best lecture Norwegian Soc of Hematology Winter meeting 2014 (7.500 NOK)

Clinical study experience

Academic trials: I have been a national coordinator for the NCMLSG's two clinical trials (Nord CML001 and 002) (Ref Prof Kimmo Porkka Helsinki Finland).

I am Study coordinator for NordCML006 (clinicaltrials.gov # NCT00852566). The study is sponsored by NTNU. This represents a substantial body of work and interaction with contract partners, sponsor, day-to-day monitoring, application preparation, interaction with regulatory authorities etc. Orally presented at ASH 2010 and 2011, and EHA 2011. I am principal investigator of NordCML007 (EudraCT number: 2011-005989-38). I am study coordinator of NordDutchCML009 (EudraCT number: 2012-004321-25). I am member of the study steering committee of EuroSKI study (EudraCT # 2011-000440-22)

I have been a regional coordinator for the Nordic Myeloma Study Group bisphosphonate study #8/2000, and taken part in many NMSG meetings. (Ref Prof Anders Waage, Trondheim)

Regional coordinator for cold hemagglutinin disease trials (Ref Prof Sigbjørn Berentsen, Haugesund sykehus)

Company trials: I have run three trials with Novartis on imatinib 2001-2003 (STI 113, 114 and 115 trials) as a regional coordinator. I have been regional coordinator for the CAMN1072303 ENESTnd trial (Nilotinib vs imatinib randomized study, N Engl J Med. 2010 Jun 17;362(24):2251-9.) Regional and national coordinator for the ENEST1st trial. Regional coordinator CLDE225 (Smo inhibitor in AML). (Ref Novartis).

I have run eight trials with Bristol Myers Squibb with their drug dasatinib (BMS-354825) 2005-2007 as a national coordinator (Ref Ms AnneMari Engström, BMS)

I have been National coordinator in Wyeths trials with SKI-606 (bosutinib) 2007-2008 (ref Dr Maria Lüttkens, Pfizer, Sweden)

I am National Coordinator for Avillion's BFORE trial

I am regional coordinator for the BYOND trial (Pfizer)

I have written and filed applications for more than 10 trials to ethics boards/ biobank regulation boards/Norwegian Medicines Agency. (Ref Central Norway Ethics Board)

Study group activities

I have been a very active member of the Norwegian Hematology Society CML group, including guidelines (see below) I have been a Norwegian member of the steering group of the Nordic CML Study (NCMLSG) group since 2004-present (Ref: Prof Bengt Simonsson, Uppsala).

I am chairman of NCMLSG since October 2010, with full responsibility for the organization. We conduct three trials (NordCML007, NordDutchCML009 and Euro-SKI) in the group presently. I organize the steering group activities, biannual group meetings, and have been involved in organization of four Nordic CML symposia. .In Oslo, 20MAR2014, I was head of arranging committee.

Lectures/PhD tuition/opposition/administrative

Lectures chairmanship: Miscellaneous lectures at hematology meetings (Norwegian, Nordic, European and American) Teaching at postgraduate courses in Norway. Chairman at different symposia, NCMLSG, Pfizer, BMS, Novartis, ARIAD, EICML etc. I was chairman of the 2014 CML education session at EHA.

Reviewer CML abstracts at American Society of Hematology (ASH) annual meetings in 2009, 2011 and chief of review committee 2012. Reviewer European Hematology Association annual meeting (EHA) 2013. Several reviews of papers to scientific journals (Blood, Leukemia, Br J Hematol, Annals of Hematology etc).

Reviewed the best Swedish hematology thesis for 2014 and 2016 for the Swedish Hematology Association Monika Klimkowska, Dept Pathology , Karolinska University Hospital Huddinge

PhD Tuition: Franz XE Gruber: 2009 Towards a quantitative understanding of CML resistance. University of Tromsø (Thesis)

Thesis opposition: Kimberley Hatfield: 2009. Angiogenic factors in human acute myeloid leukemia. University of Bergen

Bjarte Skoe Erikstein: 2012. Preclinical development of novel therapies against acute myeloid leukaemia . University of Bergen

Heidi Slåstad 2015. Large scale analysis of cellular proteins by antibody arrays. University of Oslo

Christen Lykkegaard Andersen University of Copenhagen planned for September 2017

Master tuition for MD (hovedoppgave): Ellen Rabben Leirvik and Maren Wold
Beinmargslymfocytose ved KML som prediktor for behandlingsrespons

Trondheim CML material: Wendelboe and Rønning

Norwegian EATRIS center steering board member (ESFRI initiative for translational research) (Ref Prof Kjetil Tasken, Oslo University)

Advisory committee for development of LabRoS, an electronic tool for ordering and demonstration of lab results (Pathology, medical biochemistry, radiology, microbiology, pharmacology) (Ref Marela Divic/Hilde Sveli, Tieto, Oslo, Norway)

Application for membership in European Leukemia Network (ELN) of NTNU.

Member of Board of European Science Foundation-ELN steering committee (Ref Prof R Hehlmann, Mannheim, Germany, Coordinator for ELN)

Guidelines/ Official recommendations: .

Norwegian Guidelines for CML (revised 2004, 2006, 2008, 2012, 2013, 2014 and 2016) (Ref Dr Tobias Gedde-Dahl, Rikshospitalet, Oslo).

<http://helsedirektoratet.no/publikasjoner/nasjonalt-handlingsprogram-medisninslinjer-for-diagnostikk-behandling-og-oppfolging-av-maligne-blodsykdommer/Publikasjoner/nasjonalt-handlingsprogram-maligne-blodsykdommer.pdf>

ELN Guidelines 2013: Baccarani et al I sit on the committee for the 2017 revision

Recommendations for neutropenic infections (Norwegian health directorate) 2013 Co-author (Ref: Dag Torfoss, OUS-Radiumhospitalet)

<http://helsedirektoratet.no/sites/antibiotikabruk-i-sykehus/terapikapitler/febril-noytropeni/Sider/default.aspx>

Expert advisory role for the Norwegian Medicine's Agency Legemiddelverket 2014-2016

Member of the Scientific Advisory Board for the Norwegian Cancer Association 2016-

Postgraduate courses: CML and MPD lectures at annual course in Trondheim (Hematology for Internal Medicine speciality). I chaired the course committee from 2014- present. Lectures at biannual course in malignant hematology for hematology at Oslo University Hospital

Professor competence evaluation: JAN 2013.

Head of Hematology teaching unit, Faculty of Medicine NTNU from DEC 2016

Trondheim, 15AUG2017

Henrik Hjorth-Hansen

Scientific publications:¹⁻⁵⁴

1. Abboud C, Berman E, Cohen A, Cortes J, DeAngelo D, Deininger M, *et al.* The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood* 2013; **121**: 4439-4442.
2. Baccarani M, Deininger MW, Rosti G, Hochhaus A, Soverini S, Apperley JF, *et al.* European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood* 2013; **122**: 872-884.
3. Baccarani M, Rosti G, Castagnetti F, Haznedaroglu I, Porkka K, Abruzzese E, *et al.* Comparison of imatinib 400 mg and 800 mg daily in the front-line treatment of high-risk, Philadelphia-positive chronic myeloid leukemia: a European LeukemiaNet Study. *Blood* 2009; **113**: 4497-4504.
4. Berentsen S, Randen U, Vagan AM, Hjorth-Hansen H, Vik A, Dalgaard J, *et al.* High response rate and durable remissions following fludarabine and rituximab combination therapy for chronic cold agglutinin disease. *Blood* 2010.
5. Berentsen S, Ulvestad E, Gjertsen BT, Hjorth-Hansen H, Langholm R, Knutsen H, *et al.* Rituximab for primary chronic cold agglutinin disease: a prospective study of 37 courses of therapy in 27 patients. *Blood* 2004; **103**: 2925-2928.
6. Berentsen S, Ulvestad E, Langholm R, Beiske K, Hjorth-Hansen H, Ghanima W, *et al.* Primary chronic cold agglutinin disease: a population based clinical study of 86 patients. *Haematologica* 2006; **91**: 460-466.
7. Borset M, Hjorth-Hansen H, Johnsen AC, Seidel C, Waage A, Espevik T, *et al.* Apoptosis, proliferation and NF-kappaB activation induced by agonistic Fas antibodies in the human myeloma cell line OH-2: amplification of Fas-mediated apoptosis by tumor necrosis factor. *Eur J Haematol* 1999; **63**: 345-353.
8. Borset M, Hjorth-Hansen H, Seidel C, Sundan A, Waage A. Hepatocyte growth factor and its receptor c-met in multiple myeloma. *Blood* 1996; **88**: 3998-4004.
9. Borset M, Seidel C, Hjorth-Hansen H, Waage A, Sundan A. The role of hepatocyte growth factor and its receptor c-Met in multiple myeloma and other blood malignancies. *Leuk Lymphoma* 1999; **32**: 249-256.
10. Brenne AT, Ro TB, Waage A, Sundan A, Borset M, Hjorth-Hansen H. Interleukin-21 is a growth and survival factor for human myeloma cells. *Blood* 2002; **99**: 3756-3762.
11. Christiansson L, Soderlund S, Mangsbo S, Hjorth-Hansen H, Hoglund M, Markevarn B, *et al.* The tyrosine kinase inhibitors imatinib and dasatinib reduce myeloid suppressor cells and release effector lymphocyte responses. *Mol Cancer Ther* 2015; **14**: 1181-1191.
12. El Missiry M, Adnan Awad S, Rajala HL, Al-Samadi A, Ekblom M, Markevan B, *et al.* Assessment of bone marrow lymphocytic status during tyrosine kinase inhibitor therapy and its relation to therapy response in chronic myeloid leukaemia. *J Cancer Res Clin Oncol* 2016; **142**: 1041-1050.
13. Espinosa A, Hjorth-Hansen H, Aasly K, Teigum I, Sivertsen G, Seghatchian J. Implementation of a standardised method for the production of allogeneic serum eye drops from regular blood donors in a Norwegian University Hospital: Some methodological aspects and clinical considerations. *Transfus Apher Sci* 2015.
14. Fossmark R, Skarsvag E, Aarset H, Hjorth-Hansen H, Waldum HL. Symptomatic primary (Al) amyloidosis of the stomach and duodenum. *Case Rep Gastrointest Med* 2013; **2013**: 525439.

15. Gimsing P, Carlson K, Turesson I, Fayers P, Waage A, Vangsted A, *et al.* Effect of pamidronate 30 mg versus 90 mg on physical function in patients with newly diagnosed multiple myeloma (Nordic Myeloma Study Group): a double-blind, randomised controlled trial. *Lancet Oncol* 2010; **11**: 973-982.
16. Gruber FX, Hjorth-Hansen H, Mikkola I, Stenke L, Johansen T. A novel Bcr-Abl splice isoform is associated with the L248V mutation in CML patients with acquired resistance to imatinib. *Leukemia* 2006; **20**: 2057-2060.
17. Gruber FX, Lamark T, Anonli A, Sovershaev MA, Olsen M, Gedde-Dahl T, *et al.* Selecting and deselecting imatinib-resistant clones: observations made by longitudinal, quantitative monitoring of mutated BCR-ABL. *Leukemia* 2005; **19**: 2159-2165.
18. Gruber FX, Lundan T, Goll R, Silye A, Mikkola I, Rekvig OP, *et al.* BCR-ABL isoforms associated with intrinsic or acquired resistance to imatinib: more heterogeneous than just ABL kinase domain point mutations? *MedOncol* 2011.
19. Hjertner O, Hjorth-Hansen H, Borset M, Seidel C, Waage A, Sundan A. Bone morphogenetic protein-4 inhibits proliferation and induces apoptosis of multiple myeloma cells. *Blood* 2001; **97**: 516-522.
20. Hjertner O, Qvigstad G, Hjorth-Hansen H, Seidel C, Woodliff J, Epstein J, *et al.* Expression of urokinase plasminogen activator and the urokinase plasminogen activator receptor in myeloma cells. *Br J Haematol* 2000; **109**: 815-822.
21. Hjertner O, Torgersen ML, Seidel C, Hjorth-Hansen H, Waage A, Borset M, *et al.* Hepatocyte growth factor (HGF) induces interleukin-11 secretion from osteoblasts: a possible role for HGF in myeloma-associated osteolytic bone disease. *Blood* 1999; **94**: 3883-3888.
22. Hjorth-Hansen H, Gruber F, Gedde-Dahl T. Nasjonalt handlingsprogram for kronisk myelogen leukemi. 2004.
23. Hjorth-Hansen H, Seidel C, Lamvik J, Borset M, Sundan A, Waage A. Elevated serum concentrations of hepatocyte growth factor in acute myelocytic leukaemia. *Eur J Haematol* 1999; **62**: 129-134.
24. Hjorth-Hansen H, Seifert MF, Borset M, Aarset H, Ostlie A, Sundan A, *et al.* Marked osteoblastopenia and reduced bone formation in a model of multiple myeloma bone disease in severe combined immunodeficiency mice. *J Bone Miner Res* 1999; **14**: 256-263.
25. Hjorth-Hansen H, Stenke L, Soderlund S, Dreimane A, Ehrencrona H, Gedde-Dahl T, *et al.* Dasatinib induces fast and deep responses in newly diagnosed chronic myeloid leukaemia patients in chronic phase: clinical results from a randomised phase-2 study (NordCML006). *Eur J Haematol* 2015; **94**: 243-250.
26. Hjorth-Hansen H, Stentoft J, Richter J, Koskenvesa P, Hoglund M, Dreimane A, *et al.* Safety and efficacy of the combination of pegylated interferon-alpha2b and dasatinib in newly diagnosed chronic-phase chronic myeloid leukemia patients. *Leukemia* 2016.
27. Hjorth-Hansen H, Waage A, Borset M. Interleukin-15 blocks apoptosis and induces proliferation of the human myeloma cell line OH-2 and freshly isolated myeloma cells. *Br J Haematol* 1999; **106**: 28-34.
28. Hov H, Holt RU, Ro TB, Fagerli UM, Hjorth-Hansen H, Baykov V, *et al.* A selective c-met inhibitor blocks an autocrine hepatocyte growth factor growth loop in ANBL-6 cells and prevents migration and adhesion of myeloma cells. *Clin Cancer Res* 2004; **10**: 6686-6694.
29. Ilander M, Olsson-Stromberg U, Lahteenmaki H, Kasanen T, Koskenvesa P, Soderlund S, *et al.* Disease Relapse After Tyrosine Kinase Inhibitor Treatment Discontinuation in Chronic

Myeloid Leukaemia is Related to Both Low Number and Impaired Function of NK Cells. *Scand J Immunol* 2014; **79**: 467-468.

30. Ilander MM, Olsson-Stromberg U, Lahteenmaki H, Tiina K, Koskenvesa P, Soderlund S, *et al.* Early Disease Relapse after Tyrosine Kinase Inhibitor Treatment Discontinuation in CML Is Related Both to Low Number and Impaired Function of NK-Cells. *Blood* 2014; **124**.
31. Jonsson S, Hjorth-Hansen H, Olsson B, Wadenvik H, Sundan A, Standal T. Second-generation TKI dasatinib inhibits proliferation of mesenchymal stem cells and osteoblast differentiation in vitro. *Leukemia* 2010; **24**: 1357-1359.
32. Jonsson S, Hjorth-Hansen H, Olsson B, Wadenvik H, Sundan A, Standal T. Imatinib inhibits proliferation of human mesenchymal stem cells and promotes early but not late osteoblast differentiation in vitro. *JBone MinerMetab* 2012; **30**: 119-123.
33. Koskenvesa P, Kreutzman A, Rohon P, Pihlman M, Vakkila E, Rasanen A, *et al.* Imatinib and pegylated IFN-alpha2b discontinuation in first-line chronic myeloid leukemia patients following a major molecular response. *Eur J Haematol* 2014; **92**: 413-420.
34. Kreutzman A, Jaatinen T, Greco D, Vakkila E, Richter J, Ekblom M, *et al.* Killer-cell immunoglobulin-like receptor gene profile predicts good molecular response to dasatinib therapy in chronic myeloid leukemia. *ExpHematol* 2012; **40**: 906-913.
35. Landberg N, Hansen N, Askmyr M, Agerstam H, Lassen C, Rissler M, *et al.* IL1RAP expression as a measure of leukemic stem cell burden at diagnosis of chronic myeloid leukemia predicts therapy outcome. *Leukemia* 2016; **30**: 253-257.
36. Mustjoki S, Ekblom M, Arstila TP, Dybedal I, Epling-Burnette PK, Guilhot F, *et al.* Clonal expansion of T/NK-cells during tyrosine kinase inhibitor dasatinib therapy. *Leukemia* 2009; **23**: 1398-1405.
37. Mustjoki S, Richter J, Barbany G, Ehrencrona H, Fioretos T, Gedde-Dahl T, *et al.* Impact of malignant stem cell burden on therapy outcome in newly diagnosed chronic myeloid leukemia patients. *Leukemia* 2013; **27**: 1520-1526.
38. Porkka K, Koskenvesa P, Lundan T, Rimpilainen J, Mustjoki S, Smykla R, *et al.* Dasatinib crosses the blood-brain barrier and is an efficient therapy for central nervous system Philadelphia chromosome-positive leukemia. *Blood* 2008; **112**: 1005-1012.
39. Reseland JE, Reppe S, Olstad OK, Hjorth-Hansen H, Brenne AT, Syversen U, *et al.* Abnormal adipokine levels and leptin-induced changes in gene expression profiles in multiple myeloma. *EurJHaematol* 2009; **83**: 460-470.
40. Ro TB, Holt RU, Brenne AT, Hjorth-Hansen H, Waage A, Hjertner O, *et al.* Bone morphogenetic protein-5, -6 and -7 inhibit growth and induce apoptosis in human myeloma cells. *Oncogene* 2004; **23**: 3024-3032.
41. Seidel C, Borset M, Hjertner O, Cao D, Abildgaard N, Hjorth-Hansen H, *et al.* High levels of soluble syndecan-1 in myeloma-derived bone marrow: modulation of hepatocyte growth factor activity. *Blood* 2000; **96**: 3139-3146.
42. Seidel C, Borset M, Hjorth-Hansen H, Sundan A, Waage A. Role of hepatocyte growth factor and its receptor c-met in multiple myeloma. *Med Oncol* 1998; **15**: 145-153.
43. Seidel C, Hjertner O, Abildgaard N, Heickendorff L, Hjorth M, Westin J, *et al.* Serum osteoprotegerin levels are reduced in patients with multiple myeloma with lytic bone disease. *Blood* 2001; **98**: 2269-2271.

44. Seidel C, Hjorth-Hansen H, Bendz B, Borset M, Sandset PM, Hansen JB, *et al.* Hepatocyte growth factor in serum after injection of unfractionated and low molecular weight heparin in healthy individuals. *Br J Haematol* 1999; **105**: 641-647.
45. Simonsson B, Gedde-Dahl T, Markevarn B, Remes K, Stentoft J, Almqvist A, *et al.* Combination of pegylated interferon- α 2b with imatinib increases molecular response rates in patients with low or intermediate risk chronic myeloid leukemia. *Blood* 2011.
46. Simonsson B, Hjorth-Hansen H, Bjerrum OW, Porkka K. Interferon for Treatment of Chronic Myeloid Leukemia. *Curr Drug Targets* 2010.
47. Standal T, Hjorth-Hansen H, Rasmussen T, Dahl IM, Lenhoff S, Brenne AT, *et al.* Osteopontin is an adhesive factor for myeloma cells and is found in increased levels in plasma from patients with multiple myeloma. *Haematologica* 2004; **89**: 174-182.
48. Vanky E, Hjorth-Hansen H, Carlsen SM. Metformin and early pregnancy? *Fertil Steril* 2006; **86**: 1551-1552; author reply 1552-1553.
49. Vanky E, Salvesen KA, Hjorth-Hansen H, Bjerve K, Carlsen SM. Beneficial effect of metformin on pregnancy outcome in women with polycystic ovary syndrome is not associated with major changes in C-reactive protein levels or indices of coagulation. *Fertil Steril* 2006; **85**: 770-774.
50. Vefring HK, Gruber FX, Wee L, Hovland R, Hjorth-Hansen H, Gedde Dahl T, *et al.* Chronic myelogenous leukemia with the e6a2 BCR-ABL and lacking imatinib response: presentation of two cases. *Acta Haematol* 2009; **122**: 11-16.
51. Soderlund S, Christiansson L, Persson I, Hjorth-Hansen H, Richter J, Simonsson B, *et al.* Plasma proteomics in CML patients before and after initiation of tyrosine kinase inhibitor therapy reveals induced Th1 immunity and loss of angiogenic stimuli. *Leuk Res* 2016; **50**: 95-103.
52. El Missiry M, Hjorth-Hansen H, Richter J, Olson-Stromberg U, Stenke L, Porkka K, *et al.* Early BCR-ABL1 Transcript Decline after 1 Month of Tyrosine Kinase Inhibitor Therapy as an Indicator for Treatment Response in Chronic Myeloid Leukemia. *PLoS One* 2017; **12**: e0171041.
53. Stray-Pedersen A, Sorte HS, Samarakoon P, Gambin T, Chinn IK, Coban Akdemir ZH, *et al.* Primary immunodeficiency diseases: Genomic approaches delineate heterogeneous Mendelian disorders. *J Allergy Clin Immunol* 2017; **139**: 232-245.
54. Warfvinge R, Geironsen Ulfsson L, Sommarin MN, Lang S, Karlsson C, Roschupkina T, *et al.* Single-cell molecular analysis defines therapy response and immunophenotype of stem cell subpopulations in CML. *Blood* 2017.