Curriculum vitae Arild Christian Rustan **05-2016**

Date of Birth: 9. March 1957
Degrees: MSc Pharm, D Phil (PhD)

University Education:

1981	Master of Science (Pharmacy), University of Oslo
1988	Doctor of Philosophy (Pharmacology), The Faculty of Mathematics and Natural Sciences, University of Oslo

Posts held:

1982-1988	Research Assistant, Dept. of Pharmacology, School of Pharmacy, University of Oslo
1989-1991	Post-doctoral Research Assistant, Institute for Nutrition Research, University of Oslo
1991-1995	Associate Professor, Dept. of Pharmacology, School of Pharmacy, University of Oslo
1995-	Professor (Pharmacology), Dept. of Pharmacology (now Pharmaceutical Biosciences), School of Pharmacy, University of Oslo

Scientific profile: My research has mainly been in the field of lipid and glucose metabolism in various cell culture systems. Together with professor GH Thoresen, I have established a competitive group in the field of skeletal muscle insulin resistance and are involved in several international collaborations and consortia. I have been committee member for Norwegian Research Council (FRIBIO) and served on several international evaluation panels. I am regular referee for Diabetologia, Diabetes, J. Lipid Res., PLoS One etc.

Research group: The muscle metabolism research group at Department of Pharmaceutical Biosciences, School of Pharmacy, UiO is managed by AC Rustan and GH Thoresen. The group has long term experience with the study of insulin resistance and fuel metabolism in cultured human skeletal muscle cells (myotubes). We have established a novel high throughput system for measuring fuel-handling processes in cells. This is a non-invasive method for quantifying uptake and oxidation of radiolabeled nutrients like fatty acids, monosaccharides and amino acids (Wensaas et al., J. Lipid Res 2007). Combined with real-time qPCR and genome wide screening, using microarray technology, and specific protein measurements (immunoblotting, enzyme activity assays) this allows us to study functional aspects of gene regulation.
Persons involved are professor V Aas, University College of Oslo and Akershus, ET Kase (lecturer), N Nikolic (post.doc), J Lund, NG Løvsletten (research fellows), laboratory personnel and master students.

In 2008 the research group **MURES** (Muscle research at MN, http://www.mures.uio.no), leaded by us, have been selected as an Emerging Research Initiative by the Faculty of Mathematics and Natural Sciences (MN), UiO. MURES is a collaboration between the Rustan/Thoresen group and three other research groups at MN. One PhD-student (N Nikolic) has been granted to the Rustan/Thoresen group through this initiative (also see below).

LXR antagonists innovation project: "Anti obesity" (NFR-FORNY program 2007-2009; Birkeland Innovation, UiO and Norwegian Research Council (NRC), managed by researcher ET Kase): *"New drugs for treatment of disorders associated with insulin resistance, such as type 2 diabetes and obesity"*. Focus is on the LXR antagonist 22-S-hydroxycholesterol (22-S-HC) and derivatives. Stage 2 "New drugs for treatment of obesity" of this project with focus of low molecular weight derivatives (funded by NRC, 2010-2011). We received Helse Sør-Øst Innovasjonsmidler (2012-2013) to further development of the project.

Research abroad: *1999-2000:* L. Storlien, Dept. of Biomedical Science, University of Wollongong, NSW 2522, Australia. This research stay has initiated collaboration with AstraZeneca, Mølndal,

Sweden. *Autumn 2008 and summer 2009:* SR Smith, C Moro and S Bajpeyi, Pennington Biomedical Research Center (PBRC), Baton Rouge, LA, USA. *Autumn 2015:* P. Flachs, J Kopecky, Institute of Physiology Academy of Sciences of the Czech Republic, Prague, Czech Republic. *Spring 2016:* C. Moro, Institut de Médecine Moléculaire, INSERM U858, Toulouse, France.

International network and collaboration: I have been MC member for Norway in COST-actions B5 og B17: *"Molecular Mechanisms in the Etiology of Non-Insulin Dependent Diabetes Mellitus", "Insulin resistance, obesity and diabetes mellitus in the elderly"* (NRC). **Lipgene and Nutrigenomics (NuGo):** LipGene was an EU 6th FP IP (2004-2009) entitled *"Diet, genomics and the metabolic syndrome: an integrated nutrition, agro-food, social and economic analysis"*. We were involved in workpackage *"Mechanistic studies, human adipocytes and skeletal muscle cells, and animal studies"*. **NuGo:** *"Nutrigenomics, a Network of Excellence on Nutrition and Genomics"* is a network integrating nutritional genomics in Europe through EU 6th FP. Participating in focus team *"Skeletal muscle insulin resistance"*.
I have also been MC member of **MITOFOOD** (COST-action FA0602) (2007-2011), which was a research community for nutritional optimization of mitochondrial function for health promotion and disease resistance.
Collaboration with Jagiellonian University, Krakow and R Blomhoff and RK Berge in Norway within **Polish-Norwegian Research Fund** (OPI-EAA) (2008-2011): *"The protective mechanisms against neurodegeneration: prosurvival activity of endogenous peptides, L-arginine and fatty acids as potential modulators of mitochondrial function in the stressed brain"*. I have been the Norwegian coordinator.
We have participated in an EU project **NutriTech** in collaboration with Department of Nutrition, UiO:*"Application of new technologies and methods in nutrition research – the example of phenotypic flexibility"*. (EU 7 large scale integrating project, 2012-2015), workpackage: Muscle and adipose phenotypic flexibility. At present I am MC-substitute in **MITOEAGLE**; Mitochondrial fitness mapping: Evolution - Age - Gender - Lifestyle – Environment (COST Action CA15203) (2016 -).

Most important current international collaborations: C. Moro, Institut de Médecine Moléculaire, INSERM U858, Toulouse, France. M Gaster, Odense University hospital, Denmark. S. Kersten, Wageningen University, The Netherlands, E. Ravussin, Pennington Biomedical Research Center, Baton Rouge, LA, USA. S. Bajpeyi , University of Texas at El Paso, El Paso, TX, USA. P Flachs, Institute of Physiology Academy of Sciences of the Czech Republic, Prague, Czech Republic.

Industrial link: We have established collaboration with AstraZeneca (Mølndal, Sweden) regarding cell models and development of new high-throughput methods for measurement of energy metabolism in cells. A new collaboration on innovative drug projects with muscle cells as the main cell model will be initiated in 2016-2017.

National collaborations (past and present): *Within Faculty:* The focus of the MURES group was to study skeletal muscle molecular mechanisms related to insulin resistance and type 2 diabetes mellitus (T2D). The idea of MURES was to integrate pathological human biological material and knowledge from controlled animal experiments and *in vitro* muscle cell models, with drug design as a final goal.

Department of Nutrition, School of Medicine, University of Oslo: Fatty acid-induced insulin resistance (LipGene project); muscle metabolic flexibility (NutriTech). Regulation of liver X receptors (LXR) and other nuclear receptors involved in lipid and glucose metabolism. Role of Perilipin2 in skeletal muscle.
University College of Oslo: Molecular and cellular mechanisms for skeletal muscle insulin resistance.
The Norwegian School of Sport Sciences: Molecular and cellular mechanisms for skeletal muscle insulin resistance: effects of muscle contraction. Energy metabolism in muscle cells from athletes.
Dept. of Endocrinology, Oslo University Hospital: Skeletal muscles, myokines and glucose

metabolism.
Institute for Experimental Medical Research, Ullevaal University Hospital, Oslo: Effects of leukaemia inhibitory factor (LIF) on energy metabolism.
Dept. Biomedicine, University of Bergen: Fatty acid-induced insulin resistance (cells and animal studies). Metabolic effects of thio-ether fatty acid analogues.
Medicinal Pharmacology and Toxicology, Department of Medical Biology, Faculty of Health Sciences, University of Tromsø: Drug development and moleuclar modeling.

Publications. I have 102 papers published in international peer-reviewed journals (H-index 31).
Last 5 years:

1. Lund J, Stensrud C, Rajender, Bohov P, Thoresen GH, Berge RK, Wright M, Kamal A, Rustan AC, Miller AD, Skorve J. The molecular structure of thio-ether fatty acids influences PPAR-dependent regulation of lipid metabolism. *Bioorg Med Chem. 2016 Mar 15;24(6):1191-203.*
2. Kong XY, Feng YZ, Eftestøl E, Kase ET, Haugum H, Eskild W, Rustan AC, Thoresen GH. Increased glucose utilization and decreased fatty acid metabolism in myotubes from Glmp(gt/gt) mice. *Arch Physiol Biochem. 2016 Feb;122(1):36-45.*
3. Coué M, Badin PM, Vila IK, Laurens C, Louche K, Marquès MA, Bourlier V, Mouisel E, Tavernier G, Rustan AC, Galgani JE, Joanisse DR, Smith SR, Langin D, Moro C. Defective Natriuretic Peptide Receptor Signaling in Skeletal Muscle Links Obesity to Type 2 Diabetes. *Diabetes. 2015 Dec;64(12):4033-45.*
4. Covington JD, Myland CK, Rustan AC, Ravussin E, Smith SR, Bajpeyi S. Effect of serial cell passaging in the retention of fiber type and mitochondrial content in primary human myotubes. *Obesity (Silver Spring). 2015 Dec;23(12):2414-20.*
5. Covington JD, Noland RC, Hebert RC, Masinter BS, Smith SR, Rustan AC, Ravussin E, Bajpeyi S. Perilipin 3 Differentially Regulates Skeletal Muscle Lipid Oxidation in Active, Sedentary, and Type 2 Diabetic Males. *J Clin Endocrinol Metab. 2015 Oct;100(10):3683-92.*
6. Kase ET, Feng YZ, Badin PM, Bakke SS, Laurens C, Coue M, Langin D, Gaster M, Thoresen GH, Rustan AC, Moro C. Primary defects in lipolysis and insulin action in skeletal muscle cells from type 2 diabetic individuals. *Biochim Biophys Acta. 2015 Sep;1851(9):1194-201.*
7. Feng YZ, Nikolić N, Bakke SS, Kase ET, Guderud K, Hjelmesæth J, Aas V, Rustan AC, Thoresen GH. Myotubes from lean and severely obese subjects with and without type 2 diabetes respond differently to an in vitro model of exercise. *Am J Physiol Cell Physiol. 2015 Apr 1;308(7):C548-56.*
8. Kong XY, Kase ET, Herskedal A, Schjalm C, Damme M, Nesset CK, Thoresen GH, Rustan AC, Eskild W. Lack of the Lysosomal Membrane Protein, GLMP, in Mice Results in Metabolic Dysregulation in Liver. *PLoS One. 2015 Jun 5;10(6):e0129402.*
9. Bakke SS, Feng YZ, Nikolić N, Kase ET, Moro C, Stensrud C, Damlien L, Ludahl MO, Sandbu R, Solheim BM, Rustan AC, Hjelmesæth J, Thoresen GH, Aas V. Myotubes from severely obese type 2 diabetic subjects accumulate less lipids and show higher lipolytic rate than myotubes from severely obese non-diabetic subjects. *PLoS One. 2015 Mar 19;10(3):e0119556.*
10. Høgmoen Åstrand OA, Gikling I, Sylte I, Rustan AC, Thoresen GH, Rongved P, Kase ET. Development of new LXR modulators that regulate LXR target genes and reduce lipogenesis in human cell models. *Eur J Med Chem. 2014 Mar 3;74:258-63.*
11. Kong XY, Nesset CK, Damme M, Løberg EM, Lübke T, Mæhlen J, Andersson KB, Lorenzo PI, Roos N, Thoresen GH, Rustan AC, Kase ET, Eskild W. Loss of lysosomal membrane protein NCU-G1 in mice results in spontaneous liver fibrosis with accumulation of lipofuscin and iron in Kupffer cells. *Dis Model Mech. 2014 Mar;7(3):351-62.*
12. Feng YZ, Nikolić N, Bakke SS, Boekschoten MV, Kersten S, Kase ET, Rustan AC, Thoresen GH. PPARδ activation in human myotubes increases mitochondrial fatty acid oxidative capacity and reduces glucose utilization by a switch in substrate preference. *Arch Physiol Biochem. 2014 Feb;120(1):12-21.*
13. Bajpeyi S, Myrland CK, Covington JD, Obanda D, Cefalu WT, Smith SR, Rustan AC, Ravussin E. Lipid in skeletal muscle myotubes is associated to the donors' insulin sensitivity and physical activity phenotypes. *Obesity (Silver Spring). 2014 Feb;22(2):426-34.*
14. Covington JD, Galgani JE, Moro C, LaGrange JM, Zhang Z, Rustan AC, Ravussin E, Bajpeyi S. Skeletal muscle perilipin 3 and coatomer proteins are increased following exercise and are associated with fat oxidation. *PLoS One. 2014 Mar 14;9(3):e91675.*

15. Smith R, Solberg R, Jacobsen LL, Voreland AL, Rustan AC, Thoresen GH, Johansen HT. Simvastatin inhibits glucose metabolism and legumain activity in human myotubes. *PLoS One. 2014 Jan 8;9(1):e85721.*
16. Aas V, Bakke SS, Feng YZ, Kase ET, Jensen J, Bajpeyi S, Thoresen GH, Rustan AC. Are cultured human myotubes far from home? *Cell Tissue Res. 2013 Dec;354(3):671-82*.
17. Kase ET, Nikolić N, Bakke SS, Bogen KK, Aas V, Thoresen GH, Rustan AC. Remodeling of oxidative energy metabolism by galactose improves glucose handling and metabolic switching in human skeletal muscle cells. *PLoS One. 2013;8(4):e59972.*
18. Norheim F, Gjelstad IM, Hjorth M, Vinknes KJ, Langleite TM, Holen T, Jensen J, Dalen KT, Karlsen AS, Kielland A, Rustan AC, Drevon CA. Molecular nutrition research: the modern way of performing nutritional science. *Nutrients. 2012 Dec 3;4(12):1898-944.*
19. Bakke SS, Moro C, Nikolić N, Hessvik NP, Badin PM, Lauvhaug L, Fredriksson K, Hesselink MK, Boekschoten MV, Kersten S, Gaster M, Thoresen GH, Rustan AC. Palmitic acid follows a different metabolic pathway than oleic acid in human skeletal muscle cells; lower lipolysis rate despite an increased level of adipose triglyceride lipase. *Biochim Biophys Acta. 2012 Oct;1821(10):1323-33.*
20. Fraser DA, Hessvik NP, Nikolić N, Aas V, Hanssen KF, Bøhn SK, Thoresen GH, Rustan AC. Benfotiamine increases glucose oxidation and downregulates NADPH oxidase 4 expression in cultured human myotubes exposed to both normal and high glucose concentrations. *Genes Nutr. 2012 Jul;7(3):459-69.*
21. Badin PM, Loubière C, Coonen M, Louche K, Tavernier G, Bourlier V, Mairal A, Rustan AC, Smith SR, Langin D, Moro C. Regulation of skeletal muscle lipolysis and oxidative metabolism by the co-lipase CGI-58. *J Lipid Res. 2012 May;53(5):839-48.*
22. Tranheim Kase E, Nikolić N, Pettersen Hessvik N, Fjeldheim AK, Jensen J, Thoresen GH, Rustan AC. Dietary supplementation with 22-S-hydroxycholesterol to rats reduces body weight gain and the accumulation of liver triacylglycerol. *Lipids. 2012 May;47(5):483-93.*
23. Hessvik NP, Bakke SS, Smith R, Ravna AW, Sylte I, Rustan AC, Thoresen GH, Kase ET. The liver X receptor modulator 22(S)-hydroxycholesterol exerts cell-type specific effects on lipid and glucose metabolism. *J Steroid Biochem Mol Biol. 2012 Feb;128(3-5):154-64.*
24. Nikolić N, Rhedin M, Rustan AC, Storlien L, Thoresen GH, Strömstedt M. Overexpression of PGC-1α increases fatty acid oxidative capacity of human skeletal muscle cells. *Biochem Res Int. 2012;2012:714074.*
25. Nikolić N, Bakke SS, Kase ET, Rudberg I, Flo Halle I, Rustan AC, Thoresen GH, Aas V. Electrical pulse stimulation of cultured human skeletal muscle cells as an in vitro model of exercise. *PLoS One. 2012;7(3):e33203.*
26. Ciocoiu CC, Ravna AW, Sylte I, Rustan AC, Hansen TV. Synthesis, molecular modeling studies and biological evaluation of fluorine substituted analogs of GW 501516. *Bioorg Med Chem. 2011 Dec 1;19(23):6982-8.*
27. Norheim F, Raastad T, Thiede B, Rustan AC, Drevon CA, Haugen F. Proteomic identification of secreted proteins from human skeletal muscle cells and expression in response to strength training. *Am J Physiol Endocrinol Metab. 2011 Nov;301(5):E1013-21.*
28. Thoresen GH, Hessvik NP, Bakke SS, Aas V, Rustan AC. Metabolic switching of human skeletal muscle cells in vitro. *Prostaglandins Leukot Essent Fatty Acids. 2011 Nov;85(5):227-34.*
29. Nehlin JO, Just M, Rustan AC, Gaster M. Human myotubes from myoblast cultures undergoing senescence exhibit defects in glucose and lipid metabolism. *Biogerontology. 2011 Aug;12(4):349-65.*
30. Badin PM, Louche K, Mairal A, Liebisch G, Schmitz G, Rustan AC, Smith SR, Langin D, Moro C. Altered skeletal muscle lipase expression and activity contribute to insulin resistance in humans. *Diabetes. 2011 Jun;60(6):1734-42.*
31. Sparks LM, Moro C, Ukropcova B, Bajpeyi S, Civitarese AE, Hulver MW, Thoresen GH, Rustan AC, Smith SR. Remodeling lipid metabolism and improving insulin responsiveness in human primary myotubes. *PLoS One. 2011;6(7):e21068.*