Seminar

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*Is There a Need to Develop Genetic Models that Account
for the Biological Complexity of Quantitative Traits?*

Tuesday, 17 April, 11:15 a.m.

In the Thunberg Lecture Hall
SCAS, Linneanum, Thunbergsvägen 2, Uppsala
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ABOUT ÖRJAN CARLBORG

Örjan Carlborg earned his Ph.D. from the Swedish University of Agricultural Sciences (SLU) in 2002 and then spent two years as a postdoctoral researcher at the University of Edinburgh's Roslin Institute. Before becoming Professor of Computational Genomics at Uppsala University in 2017, he worked as a researcher at the Linnaeus Centre for Bioinformatics (Uppsala University) and was Senior Lecturer/ Professor of Computational Genetics at SLU.

His research is on the genetics of complex traits. These are regulated by multiple genes and environmental factors and include, for example, human diseases and agricultural production traits. In particular, he studies how interactions between genes contribute to the phenotypes of individuals and how populations respond to natural and artificial selection.

Carlborg has received an outstanding Ph.D. thesis award from the Royal Swedish Academy of Agriculture and Forestry, a European Young Investigator Award from the European Science Foundation, a Future Research Leader Award from the Swedish Foundation for Strategic Research, the Balfour Lecture from the Genetics Society, United Kingdom, and was for five years a member of the Young Academy of Sweden.

Carlborg has published extensively on complex trait genetics, including the following works of particular relevance to his work at SCAS: Carlborg and Haley, *Nature Reviews Genetics* 5, no. 8 (2004):618–625; Carlborg *et al.*, *Nature Genetics* 38 (2006):418–420; Shen *et al.*, *PLOS Genetics* 8 (2012):e1002839; and Forsberg *et al.*, *Nature Genetics* 49 (2017):497–503.

At SCAS, Carlborg will work on an interspecies synthesis of works on genetic interactions with the aim of developing a framework to detect, model and predict such interactions in experimental data.

ABSTRACT

Most biological traits are the result of the actions and interactions of multiple genes and environmental factors. Understanding the genetic architecture of such complex traits is a grand challenge in biology. Over the past 20 years, thousands of loci affecting e.g. complex human diseases and agricultural production traits have been identified. The standard way to model the genetic contributions by these loci to the traits is to assume that they each have two variants (alleles) and the total genetic contribution to the trait is the sum of all these allelic effects. This additivity of the genetic effects within and across loci is the foundation of the core models in the current quantitative genetics paradigm. These models were developed nearly 100 years ago, before we knew how complex the biological mechanisms that determine these traits were. But despite their simplicity, they have been immensely useful to, for example, develop methods to describe how much of the trait variation in a population is due to genetics, to identify individual genes contributing to this variation and predict the immediate response of a population to a change in its living environment. We now know much more about the biological mechanisms that contribute to such traits and can experimentally identify the genetic variants altering these mechanisms. An important question in genetics is whether alternative genetic models will be able to use this information more efficiently to, for example, improve our ability to dissect the genetic mechanisms that contribute to the variation of complex traits and diseases, and predict the phenotypes of individuals in populations.

During the past 20 years, I have worked on studying the basis of non-additive genetic inheritance and how individual – or combinations of - loci contribute to this. Most of the work has been performed in domestic animals. More recently, work with public datasets from a range of species from yeast to plants has become more important as this has facilitated more in-depth explorations of complex inheritance patterns that could not be studied in vertebrates. Here at SCAS, my focus is on performing an in-depth theoretical and conceptual synthesis of the types of experimentally revealed inheritance mechanisms that challenge the current additive-model based paradigm in genetics. The

work aims to deliver useful illustrations of how the choice of genetic modeling strategy in the analyses of experimental data (i.e. the often implicit prior assumptions about the genetic architecture of a trait) affects the reported outcomes of the study. This is to illustrate which insights can, and which cannot, be confidently inferred from current experimental genetic studies. It will also illustrate how taking an interspecies approach to fundamental genetic problems can reveal novel insights to the genetic basis of phenotypic variation that cannot be obtained using data from one single species.

In this seminar, I will introduce and discuss the ongoing work within this project.