Building bridges over disciplinary boundaries - Experiences with the PharmaTox Strategic Research Initiative at the MN faculty

PharmaTox
STRATEGIC RESEARCH INITIATIVE

Professor Hedvig Nordeng, School of Pharmacy, UiO

Workshop Convergence Environments
28th – 29th September 2016

"**Convergence** in research and education entails a ground-breaking integration through **extensive collaboration among researchers from different disciplines** with the aim of creating new areas of knowledge, new applications and opportunities."

Why MN Strategic Research Initiative?

Driver: Renewal in **research** and **education**

- ✓ Collaboration across Institutes and disciplines
- ✓ Educating students to meet tomorrow's challenges in pharmaceuticals

Promotion of the MN Faculty

- ✓ as an **international research** faculty within "**LIFE SCIENCES**"
- ✓ as a Faculty that promotes solutions relevant for society
- ✓ as a Faculty who attracts and supports young research talents
- ✓ as a Faculty that has sharp goals and values High-risk/High Gain projects

We believe….

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- Many of the greatest challenges and opportunities that we face cannot be addressed simply within the confines of the classical disciplines.
- Progress depends on combining the expertise from diverse disciplines, and thus the modern university has to facilitate these cross-disciplinary collaborations if it is to remain at the cutting edge of human knowledge and innovation.

We believe…..

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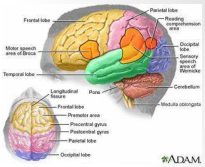
- Your specific approach and knowledge may be standard for your discipline but novel in other fields. Applying your knowledge in this new field can give you a leading advantage and a unique angle to solving outstanding problems.
- By teaming up with complementary research groups one can gain synergy. This results in increased chances in original (high-impact) research.

Why pharmaceuticals & neurodevelopment?



Major birth defects 3-5% [1]

Neurodevelopmental Behavioral Disorders 16% [2]

- Common
- Costly
- Can cause lifelong disability
- **Causes are mostly unknown!**

Identifying environmental risk factors → hope for prevention!

[1] Nilsen et al 2009 [2] Egger & Angold 2006

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2013: 1st «Endringsmiljø» proposal «PharmaSafe»

The Faculty Management's recommendation on the PharmaSafe proposal was to create a broader platform with researchers at other MN institutes (**epigenetics, statistics and bioinformatics** were specifically mentioned) and submit an Endringsmiljø-proposal in 2014.

The process leading up to PharmaTox

PharmaTox will be
joining forces across disciplines at MN
to generate novel insights
into the effects of pharmaceuticals
on neurotoxicity and neurodevelopment

The **PharmaTox** Strategic Research Initiative

Specialists in pharmacology, neurotoxicity, statistics, bioinformatics, epidemiology and epigenetics

Kick-off meeting Oct 2015

UiO

The Prescription Registry

All filled prescriptions in Norway since 2004

The MoBa-cohort

N=108 000 incl.
> 30 000 siblings

The MoBa-biobank

DNA from 90 000 children

The Medical Birth Registry

The National Patient Registry

All child diagnosis i.e. ADHD diagnosis

UNIQUE DATA SOURCES

Bjornstad S, Austdal LP, Roald B, Glover JC, Paulsen RE.
Cracking the egg:
Potential of the developing chicken as a model system for non-clinical safety studies of pharmaceuticals.
J Pharmacol Exp Ther. 2015 Oct 2.

DAGENS Medisin — Nyheter | Debatt | DM Arena | DMTV

ULIKE LEGEMIDLER: Kyllingen har blitt behandlet med forskjellige klinisk relevante legemidler . forteller farmasøyt Lars Peter Austdal og lege Sigrid Bjørnstad. **Foto:** Privat

FORSKNING

Kylling kan gi tryggere medisiner for gravide

Kyllingen har egenskaper som gjør den velegnet for studier på medisiner til gravide og til premature barn, sier lege Sigrid Bjørnstad og farmasøyt Lars Peter Austdal.

Fremtidens medisin bygger på epigenetikk

RAGNHILD ESKELAND ha… oppdaget at spesifikke ge… ner i kreftceller fra pasient… med spiserørskreft, er pak… ket inn på en annen måte enn i friske celler.

Epigenetikk

The technology

Illumina 450K platform

In collaboration with the laboratory at the Norwegian Sequencing Center

Genome-wide DNA-methylation analyses 450K Infinium Methylation BeadChip:

Currently provides the best balance between cost and distribution of genomic regions covered.

This assay enables single-base resolution quantitative measurement of DNA methylation at >450,000 CpG loci covering >30 000 transcripts.

Approach: Big Data analysis

"The challenge is not data size, but getting the right information out of it"

GK Sandve

Published online 30 April 2013 *Nucleic Acids Research, 2013, Vol. 41, Web Server issue* ***W133–W141***
doi:10.1093/nar/gkt342

The Genomic HyperBrowser: an analysis web server for genome-scale data

Geir K. Sandve[1,2], Sveinung Gundersen[3], Morten Johansen[4], Ingrid K. Glad[5], Krishanthi Gunathasan[6], Lars Holden[7], Marit Holden[7], Knut Liestøl[1,2], Ståle Nygård[8], Vegard Nygaard[4], Jonas Paulsen[1,4], Halfdan Rydbeck[1,3,7], Kai Trengereid[1], Trevor Clancy[3], Finn Drabløs[9], Egil Ferkingstad[7], Matúš Kalaš[10,11], Tonje Lien[5], Morten B. Rye[9], Arnoldo Frigessi[7,12] and Eivind Hovig[1,3,4,7,*]

The PhD students

- Multidiciplinary research requires a new type of flexible junior scientists who can bridge the gaps by combining the expertise and skills from different fields.
- It produces new scientists with unique skill sets which are of vital importance in future R&D careers in both industry and academia!

Challenges….

Interdisciplinary endeavors tend to be slower and more cumbersome to start up than projects or programs within already established scientific fields.

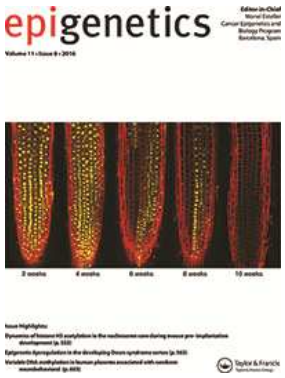
→ Ample **time** is needed for the participating researchers to learn about each others perspectives and approaches, to develop common tools to handle interdisciplinarity and to shape **efficient meeting places**.


MR. COFFEE

Excellence within our own fields

Multidisciplinary research can pose challenges when trying to get results published.

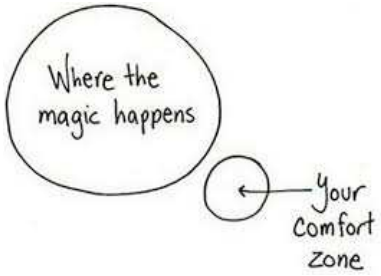
Amundsen et al. **March 2015 (IF: 18.4)**



Gervin et al. **Sept 2016** (IF: 5.3)

Final words…….

- Multidisciplinary science requires a certain mindset, openness for collaborations and capability to set aside your ego and share credit.



October 28th 2016, 09:30-15:00
Auditorium 2, 3rd floor
School of Pharmacy
University of Oslo

PharmaTox
STRATEGIC RESEARCH INITIATIVE

Open seminar series

Effects of Pharmaceuticals on Human Development and Neurotoxicity

Attendance is free and open for everybody
Registration: r.g.berge@farmasi.uio.no
or: nettskjema.uio.no/answer/74186.html
Registration deadline: October 1st 2016

Program

09:30-09:40	Welcome: The PharmaTox initiative Hedvig Nordeng
09:40-10:10	Three PharmaTox-researchers (10 min x 3): Methods in causal inference in drug safety studies Mollie Wood Emil Aas Stoltenberg Stefania Salvatore
10:10-10:40	Sources of bias in medication studies in pregnancy - results from the Danish Mother and Child Cohort Katrine Strandberg-Larsen
10:40-11:10	Antidepressants in pregnancy and offspring autism-challenges inferring causality Dheeraj Rai
11:10-12:00	Lunch
12:00-12:30	Brain and cognitive development of children born to mothers with opioid- and polysubstance use Kristine Walhovd
12:30-13:00	Epigenetic effects of drugs Kristina Gervin & Robert Lyle
13:00-13:30	What can human embryonic stem cells and IPSC teach us about neurotoxicity? Hege Brincker Ferdingstad & Ragnhild Eskeland
13:30-13.45	Break
13:40-14:10	Mechanism of drug neurotoxicity – an overview Ragnhild Paulsen
14:10-14:40	The chicken embryo – a model for drug neurotoxicity Joel Glover
14:40-14:50	Summary – the way onwards for PharmaTox Hedvig Nordeng
15:00-22:00	REAL MORO! The Faculty of Mathematics & Natural Sciences, UiO

On behalf of the PharmaTox Strategic Research Initiative:
Hedvig Nordeng Ragnhild Eskeland Ragnhild Paulsen
Geir Kjetil Sandve Sven Ove Samuelsen Robert Lyle

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The Research Council of Norway
UiO : University of Oslo
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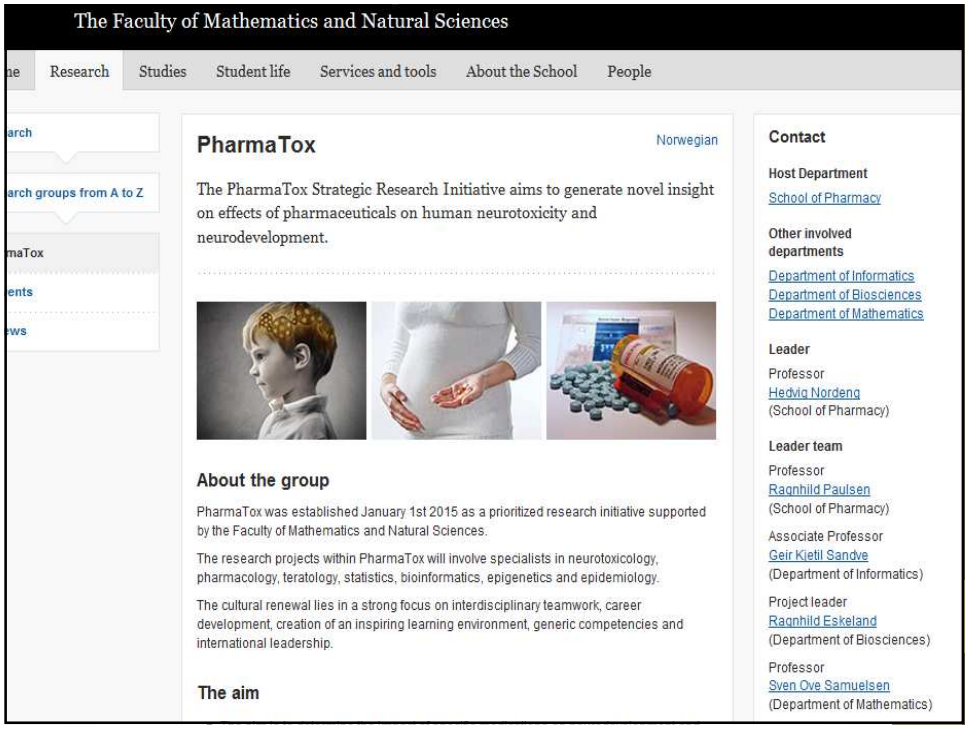

Strengths

1. Novelty of research focus enables good opportunities for novel findings/ high impact research
2. Access to unique data and models
   - *Moba-study, MoBa-biobank, Chicken Model*
3. The multidisciplinary approach and expertise
   - *From molecular neurotoxicity to epidemiology*
   - *Good mixture of young research talents and experienced researchers*
   - *Recruitment of excellent PhD/post docs*
   - *PIs show high dedication to the collaboration (study trip and high frequency of leader group meeting)*
   - *Efficient logistics for collaboration (geographic location)*
4. Research topic enables us to seek large grants
   - *ERC StG, NFR , INTPART*
5. A cost-efficient technology and laboratory facilities

PharmaTox will

- be joining forces across disciplines at MN to generate innovative and novel insights into the **effects of pharmaceuticals on neurotoxicity and neurodevelopment.**
- develop novel **statistical methodology** for the study of genotype-phenotype relations, implemented in **versatile software systems** using epidemiological and epigenetic data from MoBa as a driving application.
- use a **CNS safety pharmacology model** and **human embryonic stem cells** to give biological plausible molecular and cellular mechanisms of drug neurotoxicity.

Stem cells | **In vivo models** | **Biomarkers** | **Humans**

Advanced statistics & Bioinformatics

One platform – 3 work packages

WP1

Post doc1: Pharmaco-epidemiological studies HUMAN OBSERVATIONAL DATA

WP2

PhD2: Pharmaco-epigenetic studies HUMAN CORD BLOOD

PhD3: MECHANISTIC STUDIES: Pharmaco-epigenetics HUMAN STEM CELLS

WP3

Post doc4: MECHANISTIC STUDIES: Neurotoxicity IN OVO MODELS

PhD5 and 6: Mathematics and Medical Bioinformatics





An integrated approach:
Results form one WP will act as as hypothesis generators for the others, and vice versa