

Screening plasma biomarkers for MCI and AD by quantitative proteomic methods

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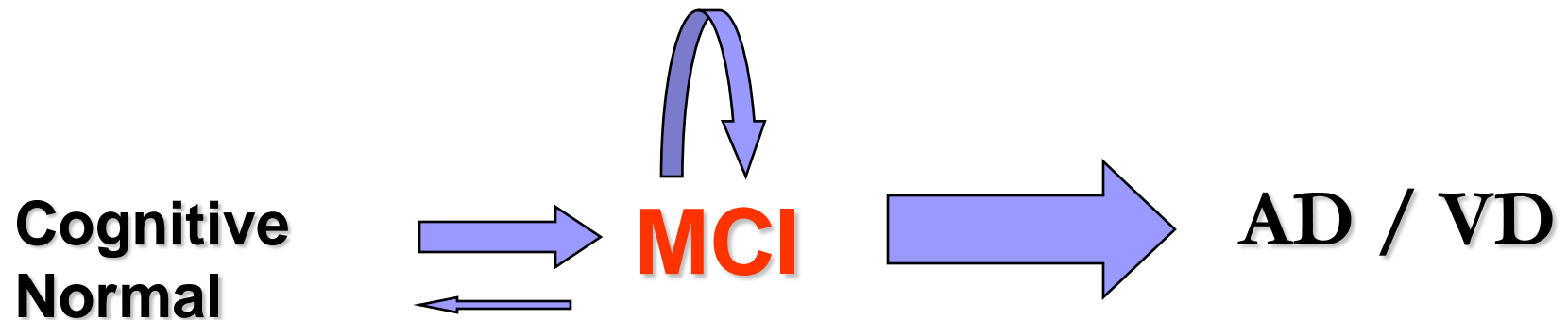
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Introduction



Annual conversion ranges from 2.7% to 15%. (Ganguli 2004, Petersen 2001)

Seven times more likely to develop AD. (Boyle et al 2006)

Fast , accurate and effective diagnostic methods for MCI are critically needed.

MCI- mild cognitive impairment

AD- Alzheimer's disease

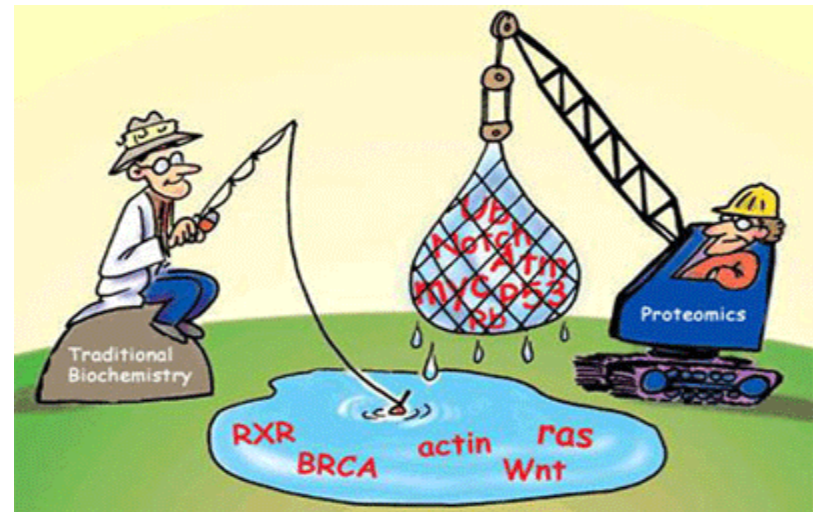
Markers for MCI and AD

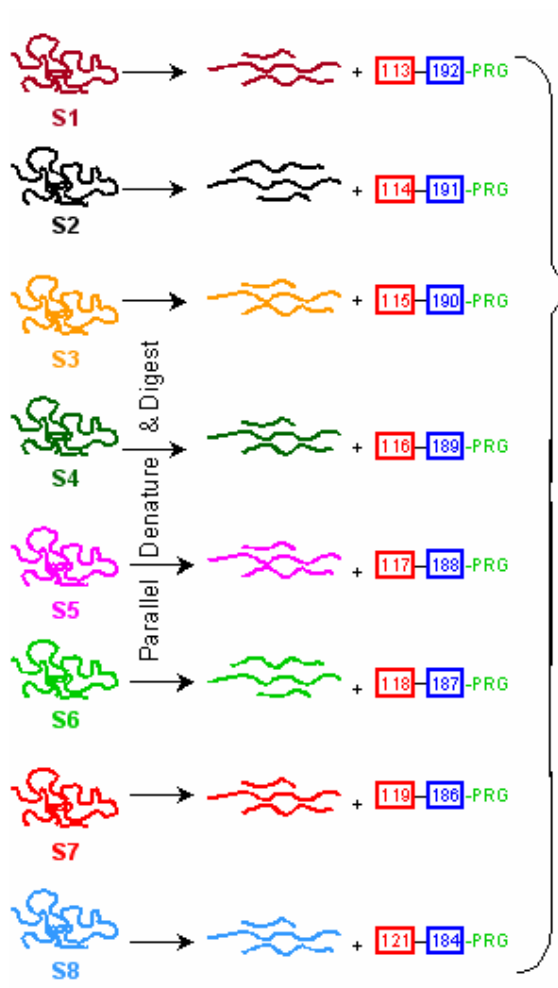
- Neuroimaging
MRI/PET expensive equipments
- Cerebrospinal fluid (CSF)
lumbar puncture, invasive
- Plasma
accessible, innocuous,
500ml of CSF absorbed into blood
best resource for early diagnosis



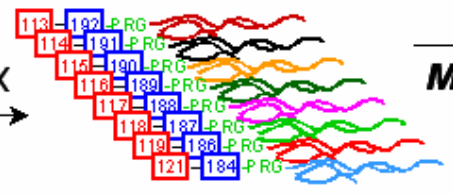
Proteomics: new techniques for analyzing proteins

- Analyze proteins in an automated, large-scale mode. No targeted biomarkers. (300 proteins)
- Focus on low abundant proteins in plasma
- Quantitative methods iTRAQ
(isobaric tag for relative and absolute quantitation)

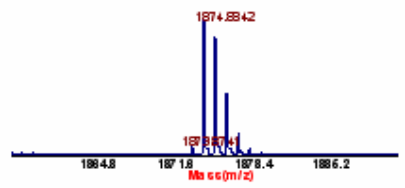




Mix
MS



-Reporter-Balance-Peptide INTACT
- 8 samples *identical m/z*

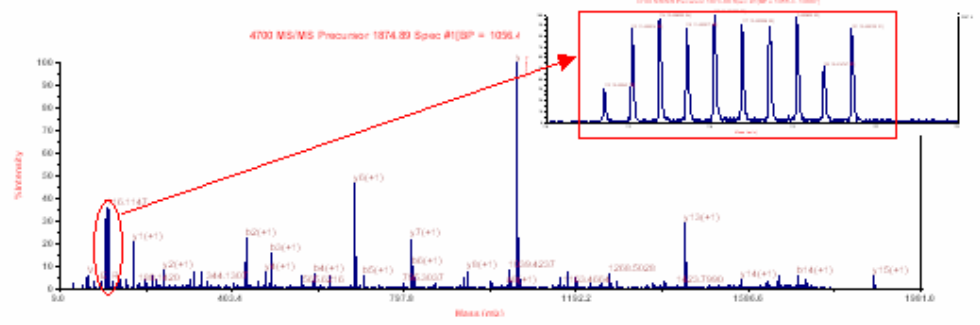


MS/MS

- 113
- 114
- 115
- 116
- 117
- 118
- 119
- 121



- Reporter ions DIFFERENT
- Peptide fragments EQUAL



Experiment 1

iTRAQ tag	113	114	115	116	117	118	119	121
group	Normal 1	Normal 2	Normal 3	aMCI	nMCI	amd MCI	nmd MCI	AD
Subjects No.	134	139	137	79	92	71	20	19

Experiment 2

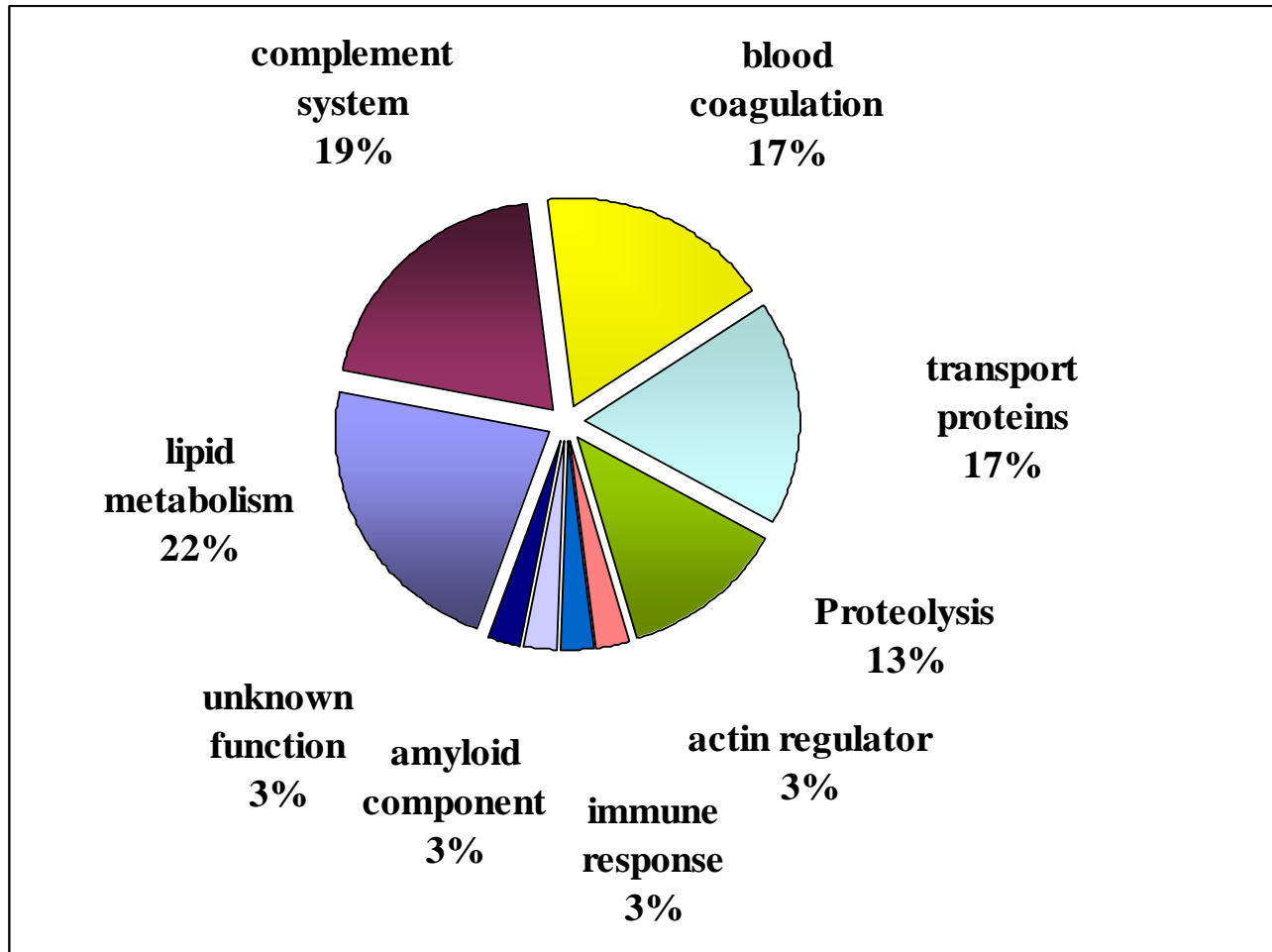
iTRAQ tag	113	114	115	116	117
group	Normal	AMCI (aMCI+amd MCI)	NMCI (nMCI+nmdMCI)	AD	nm
Subjects No.	410	150	112	19	20

Results

	abnormal regulated proteins	total proteins
1 st iTRAQ	73	219
2 nd iTRAQ	59	301

- 40 overlapped up / down regulated proteins in two iTRAQ experiments

Functions of overlapped abnormal regulated proteins



Stories behind proteins

- Inflammation

Inflammatory mechanisms are involved in the aetiology of AD, even before fibrillar amyloid deposits are present.

(Akiyama et al 2000;Veerhuis et al 2003)

complement system; proteolysis proteins

- Cardiovascular risk factor in AD pathology

lipoprotein metabolism

blood coagulation



Experiments in future

- Reconfirm potential biomarkers by other methods and individual samples, such as western-blotting and ELISA
- Test potential biomarkers in wave 2 samples of MAS study
- Verify sensitivity and specificity of potential biomarkers

Acknowledgement

- Perminder Sachdev
- Anne Poljak
- George Smythe



Bioanalytical Mass Spectrometry Facility

- Tharusha Jayasena
- Mark Raftery
- Ling Zhong
- Lewis Adler

Memory and aging institute

- Nicole Kochan
- John Crawford
- Christan Kang

South-East Area Laboratory Service

- Ora Lux Peter Day



- All research is a long way to the end.
- But nothing can stop us trying.

Thanks for your attention.