

**Proteomics International**

LABORATORIES LTD

Corporate Introduction

| India Trade Visit

| 8<sup>th</sup> - 12<sup>th</sup> May 2017

**Global leader in  
protein analysis**

Richard Lipscombe PhD  
Managing Director  
Proteomics International



# Introduction

## Corporate overview

- ▶ Diagnostics & Biomarkers
    - PromarkerD
    - Companion diagnostics
  - ▶ Analytical services
    - Biosimilars testing
    - Pharmacokinetic testing (PK)
    - Truth-in-labelling
    - 2-tag technology
  - ▶ Drug discovery
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# Corporate overview

- ▶ Revenue generating Company – Established 2001
- ▶ Listed on Australian Stock Exchange April 2015 (code: PIQ)
- ▶ Global leader & innovator in the field of proteomics
- ▶ Proven technology with established IP
- ▶ Operates from purpose built, **state-of-the art facilities** at the Harry Perkins Institute of Medical Research in Perth, Western Australia
- ▶ Business model uses proprietary technology platform which drives three synergistic proteomics-based business units in high growth markets

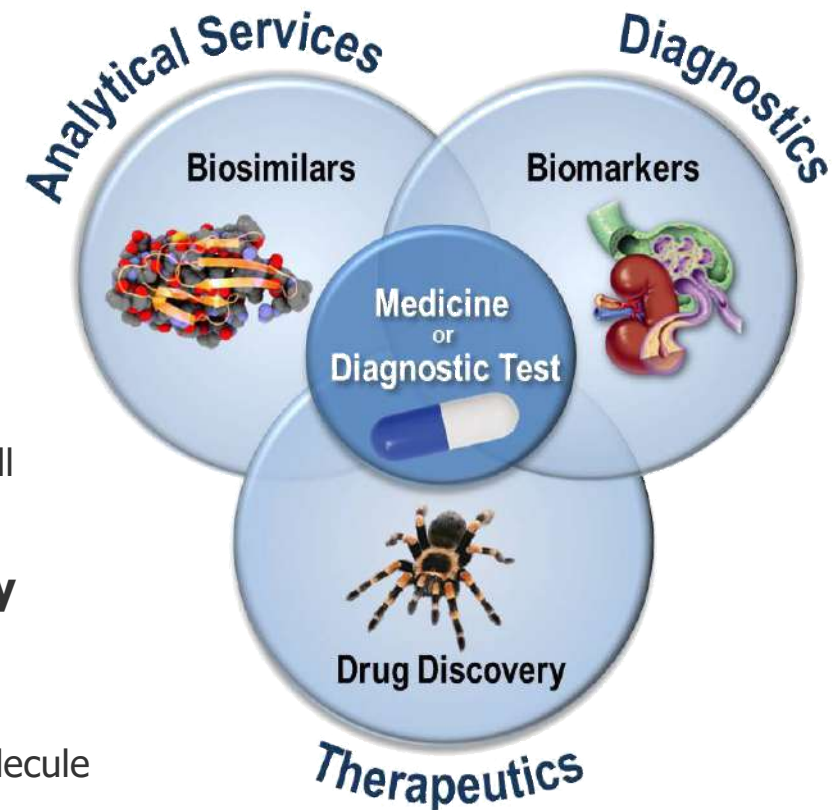


Quality is Assured



# Business model – engaged in high growth markets

- ▶ Three **synergistic business units**
- ▶ Unifying “**Promarker**” platform technology
  - leverage & efficiency
- ▶ **Diagnostics (biomarkers) market is \$24.1bn<sup>1</sup>**
  - predicted to reach \$45.6bn by 2020<sup>1</sup>
  - ‘Omics’ technology holds ~75% share.
- ▶ **Analytics (proteomics) market to be \$20.8bn by 2018<sup>2</sup>**
  - Bio-engineered protein drugs was \$152bn (2013) CAGR 7.2%
  - between 2013 & 2017, drugs worth \$50bn p.a. in revenues will come off patent
- ▶ **Therapeutics peptide based drug market currently \$17bn<sup>3</sup>**
  - 7 of world's top 10 selling drugs were proteins therapeutics
  - growing at 10%; better safety levels than traditional small molecule drugs
- ▶ Existing **revenue generation & deal flow**
  - multiple major upside opportunities



# Accreditation

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Quality is Assured

- ▶ **World's first company** to receive ISO 17025 laboratory accreditation for proteomics services
- ▶ The ISO 17025 laboratory standard ensures laboratories generate **technically valid results**, and is the most widely used laboratory standard for USA federal testing laboratories:  
[www.fda.gov/RegulatoryInformation/Guidances/ucm125434.htm](http://www.fda.gov/RegulatoryInformation/Guidances/ucm125434.htm)
- ▶ Data analysis is undertaken in accordance with the standards of:
  - **ISO/IEC 17025:2005 (Chemical Testing); and**
  - **ISO/IEC 17025:2005 (Research and Development)**
- ▶ The management of research projects is conducted in accordance with the **OECD Principles of Good Laboratory Practice**
- ▶ The facilities, methods and protocols used along with the services provided by PI are **NATA accredited**

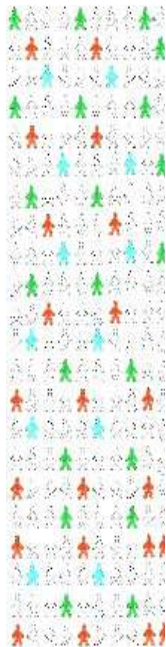


Accreditation No: 16838

# Promarker™ platform technology

One **proven and proprietary** platform, multiple uses:

- ▶ Diagnostics - biomarker discovery
- ▶ Analytics – biosimilars & pharmacokinetic testing
- ▶ Therapeutics - drug discovery



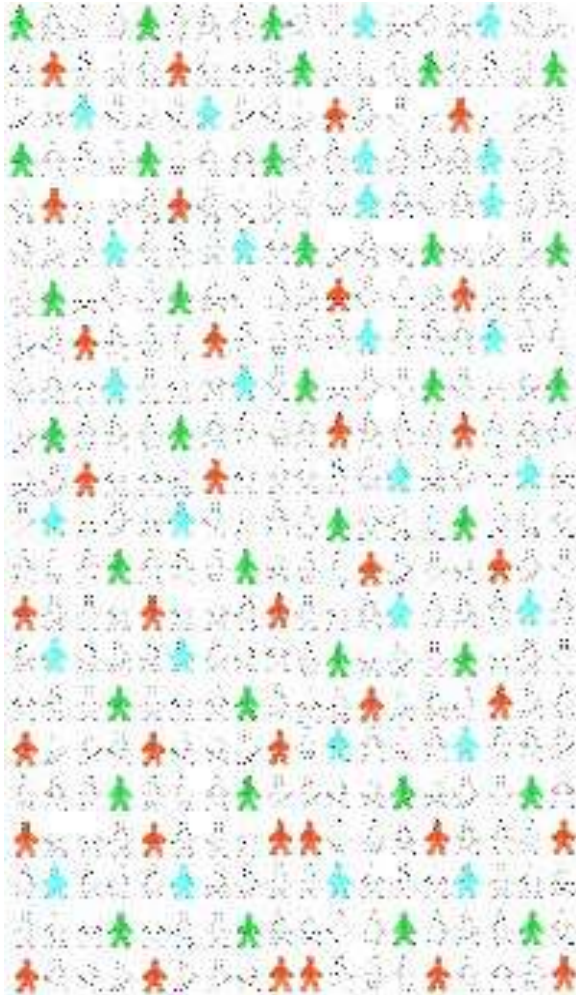
**The methodology was developed as part of a \$8m self-funded R&D program**

## Diagnostics & Biomarkers



# Biomarker discovery for new diagnostic development

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- The Question - What are we trying to find biomarkers for?
- The Cohort - Do we have the range of samples we need?
- The Process - Using our Promarker platform to answer the clinical/biological question and produce a panel of biomarkers
- Cross Validation - Cross checking our panel of biomarkers for reproducibility

# The test

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Unique protein biomarker signatures



Identification of Disease or Condition

# Current projects: Diagnostics in development

## *Diagnostic Biomarker Projects*

### Lung Conditions

- COPD accounted for approximately 3% of global disease burden and 5.5% of deaths worldwide (2011).
- Over 600,000 Australians had COPD in 2015.
- **For yearly healthcare costs for the patient and the healthcare system in 2011, this translated to over \$70 bn in Europe; \$65 bn in USA and \$1bn in Australia.**
- 2.5 million Australians suffered from asthma in 2015.
- Lost productivity cost of asthma in Australia was over \$1.1 bn in 2015.
- The cost to health system for asthma was \$1.2 bn in 2015.



### Asbestos Related Conditions

- Globally, 107,000 people die from asbestos related diseases.
- Of this, 59,000 die from mesothelioma.
- Australian deaths from mesothelioma in 2014 exceeded 600.
- As only 16% of the world's population have banned asbestos products, the incidence is expected to rise.
- **The predicted global economic cost of mesothelioma, \$2.4 bn, is likely to be understated.**
- In 2013, the global economic cost of mesothelioma was \$1.6 billion.



### Endometriosis

- 1 in 10 women worldwide are affected by endometriosis during their reproductive ages (15-49).
- 30-55% of women with endometriosis may experience infertility.
- 30-66% of women with endometriosis have an increased risk of developing ovarian cancer.
- The cost of endometriosis per woman per year is the same as the cost of diabetes.
- **The cost to Australian society is \$7.7 bn annually, with two thirds attributed to a loss of productivity.**



### Parasites

- Giardiasis affects 10% of the global population.
- **The global enteric diseases testing market will reach \$3.6 bn by 2019.**
- Successful commercialization will generate royalty streams of 5% from net sales and 50% from sub-licences.



## Case study: PromarkerD



# A world leading predictive diagnostic test - PromarkerD



Without PromarkerD



With PromarkerD



# PromarkerD in brief

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## Predictive diagnostic test for diabetic kidney disease

### The Problem

- International Diabetes Foundation estimates **415 million people** globally have diabetes
- According to US Centre for Disease Control, **35% of adults with diabetes have chronic kidney disease**; there is **no early detection test** currently available

### The Solution

- Clinical study: 576 diabetic patients followed for 4 years
- A standard blood test used to produce a protein “fingerprint”

PromarkerD **predicted** 95% of the patients who were previously kidney-disease free and go on to develop chronic kidney disease

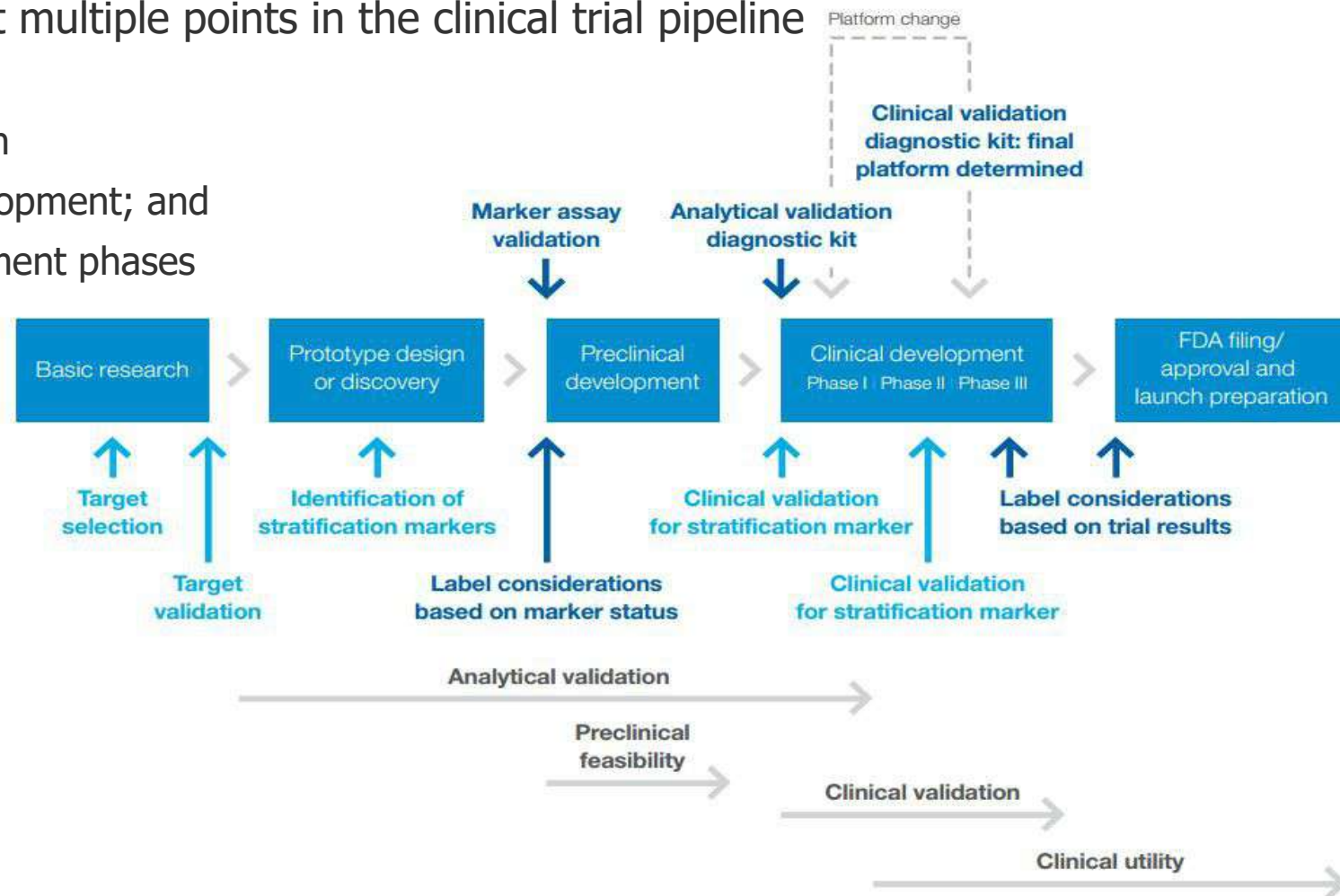


## Companion Diagnostics (CDx)



# Companion diagnostics (CDx)

- ▶ CDx is a biomarker diagnostic test to assess if a patient responds favourably to a drug or not
- ▶ Testing occurs at multiple points in the clinical trial pipeline
  - basic research
  - prototype design
  - preclinical development; and
  - clinical development phases

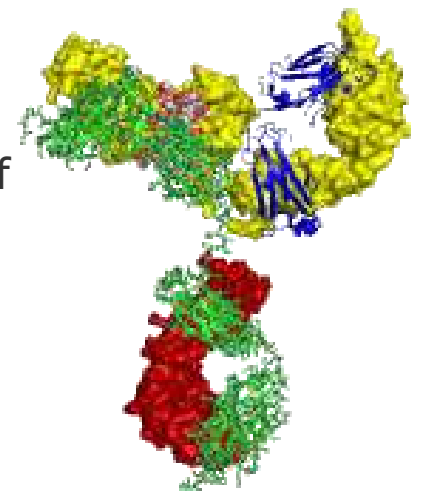


## Analytical Services



# Analytics - specialised services

- ▶ PI - one of the **world's only internationally accredited laboratories** for proteomics analysis
- ▶ Business **leverages PI's proteomics technology** platform
  - test & validate protein composition of a wide range of products
- ▶ Major applications in
  - biomarker discovery
  - companion diagnostics
  - clinical trials testing (pharmacokinetic studies)
  - food QC testing (truth in labelling)
  - generic drug market (biosimilars and biologics QC)
- ▶ 12 protein-based drugs with **combined revenue of \$50bn** will come off patent by 2017
  - driving a booming generics industry in the world's emerging economies
- ▶ Biosimilars require **rigorous testing** prior to receiving regulatory approval for commercial use
  - **part of PI's specialist service offering**



## Biosimilars & Biologics



# QA/QC for characterising biologics

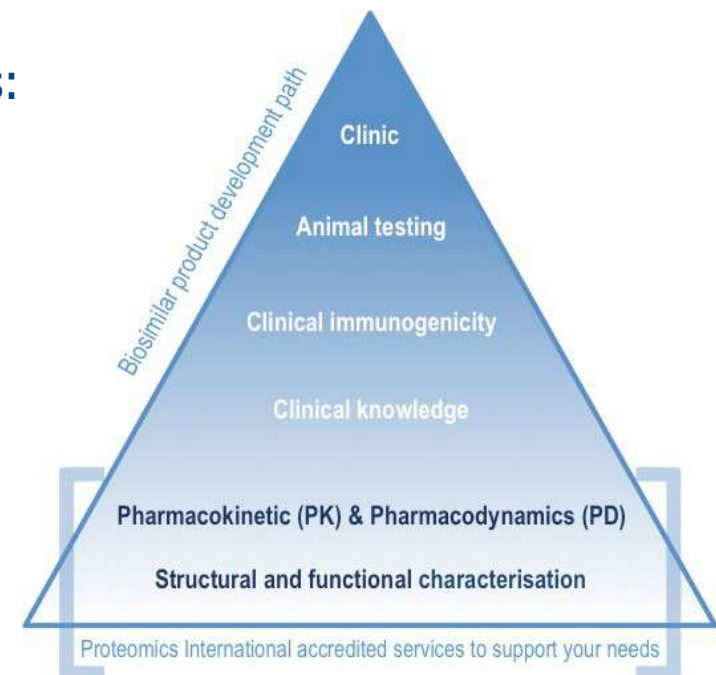
“A biosimilar product is a biological product that is approved based on a showing that it is highly similar to a FDA-approved biological product, known as a reference product. The latest FDA guidance for biosimilars states that products “with fingerprint-like similarity” permit a very high level of confidence.

## Demonstrating biosimilarity

QC characterisation requirements – ICH Q6B guidelines:

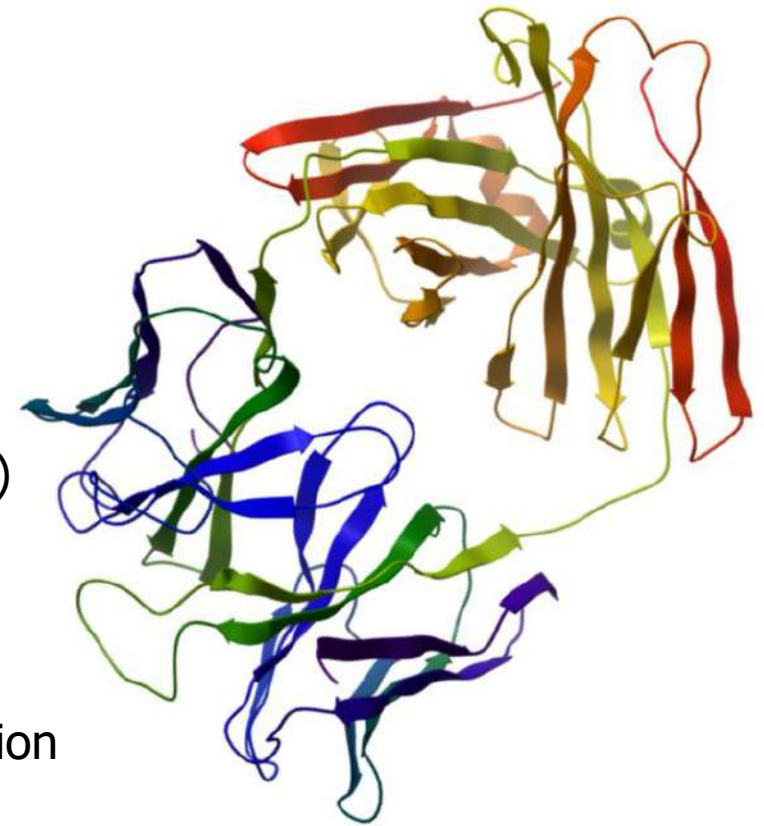
- The protein drug class is well characterised
- Characterisation is performed along side the reference product
- Extensive comparability study is carried out prior to any clinical assessment

QC validation is best done by an accredited 3rd party



## Analyses required to demonstrate biosimilarity

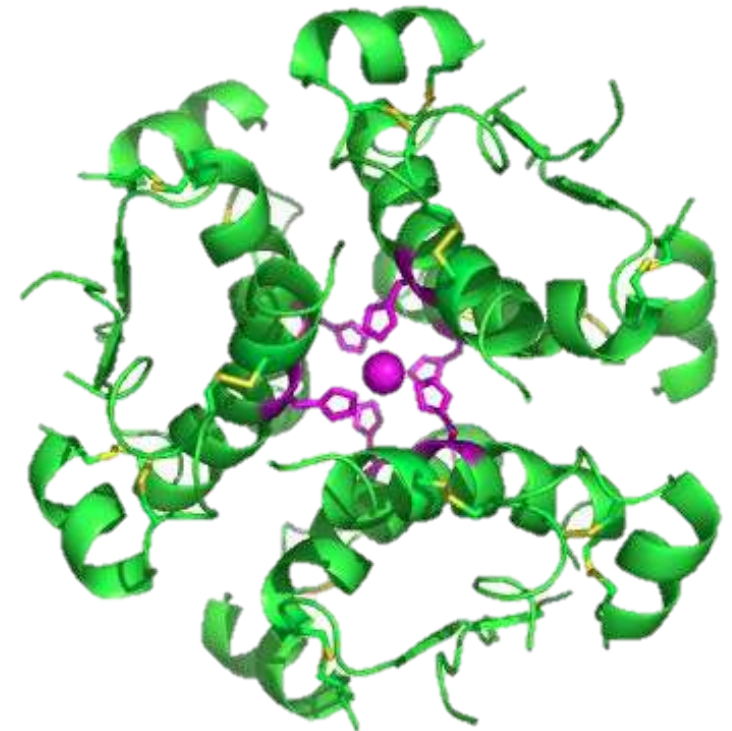
- Protein sequence mapping
- Intact mass determination
- N/C-terminal sequencing by mass spectrometry
- N-terminal (Edman) sequencing
- Amino acid analysis
- Disulphide mapping
- Impurity profiling (Met oxidation and deamidation)
- PEGylation analysis
- Glycosylation analysis
- Aggregation analysis by analytical ultracentrifugation
- Circular dichroism and X-ray crystallography
- Stability testing of new drug substances and products



# Proven biosimilars expertise

**PI has successfully undertaken a wide range of Biosimilars projects, including:**

- Human Insulin and its analogues
- mAb (Rituximab, IgG1, IgG4.....)
- Follicle Stimulating Hormone (FSH)
- Urinary trypsin inhibitor (UTI)
- Human Growth Hormone (hGH)
- Granulocyte Colony-Stimulating Factor (GCSF)
- Epidermal Growth Factor (EGF)
- Cyclic peptides (Eptifibatide and Octreotide)



Several of the data packages have been used for regulatory submission in the USA, Europe, India and China

All projects are tailored to meet specific client requirements

## Pharmacokinetic testing (PK)



# Pharmacokinetic testing (PK)

- ▶ The company offers PK testing to determine
  - bodily absorption
  - distribution
  - metabolism; and
  - excretion of drugs
- ▶ Conventional methods use ELISA
  - requires antibody generation
  - can take 3-6 months
- ▶ Mass spectrometry based testing
  - do not require antibody generation
  - faster results
- ▶ Testing is undertaken in accordance with the principles of GLP



## Truth-in- labelling



# Truth-in-labelling

- ▶ Fair trading laws and food laws in Australia<sup>1</sup> and New Zealand<sup>2,3</sup> require that labels do not misinform consumers
  - correct name or description that indicates the true nature of the food
  - accurate weights and measures information
- ▶ Proteomics International offers QC testing for food products
- ▶ Analytical services contract with The a2 Milk Company
- ▶ Protein analysis for the a2 Milk brand of fresh milk products to
  - validate protein composition; and
  - for quality control purposes
- ▶ Testing is undertaken in accordance with the principles of GLP



## Drug Discovery



# Drug Discovery

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## Targeted drug discovery from venom

- ▶ The Company has successfully used its platform technology to **discover 5 lead compounds** (peptides)
- ▶ The platform technology and proprietary software algorithm allow candidates to be tested in **months rather than years**
- ▶ Pilot study demonstrated **100 times more efficiency** in the drug discovery process than the industry normal success rate
- ▶ **Access agreement** with the Northern Territory, Australia
- ▶ *PILL's drug discovery program will enable rapid screening and an early advance of candidates to testing models, pre-clinical development and the path towards out-licensing*



# Contact us



## Proteomics International

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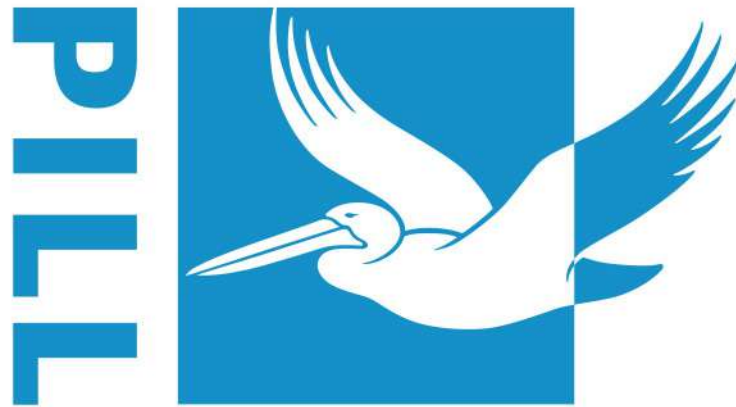
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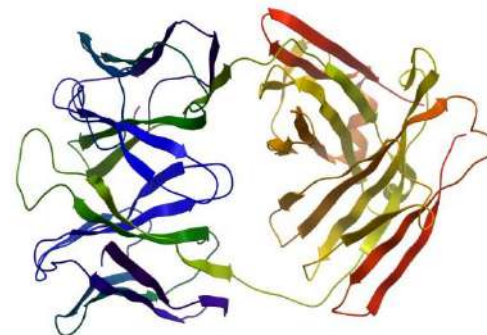
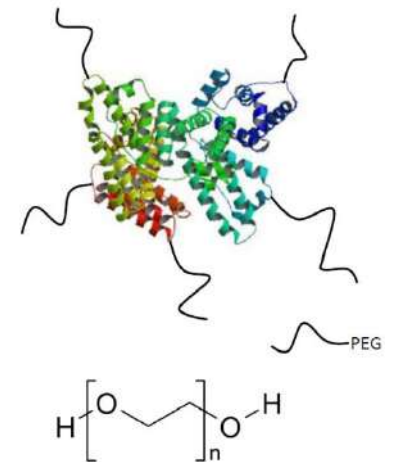
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# Characterisation analysis

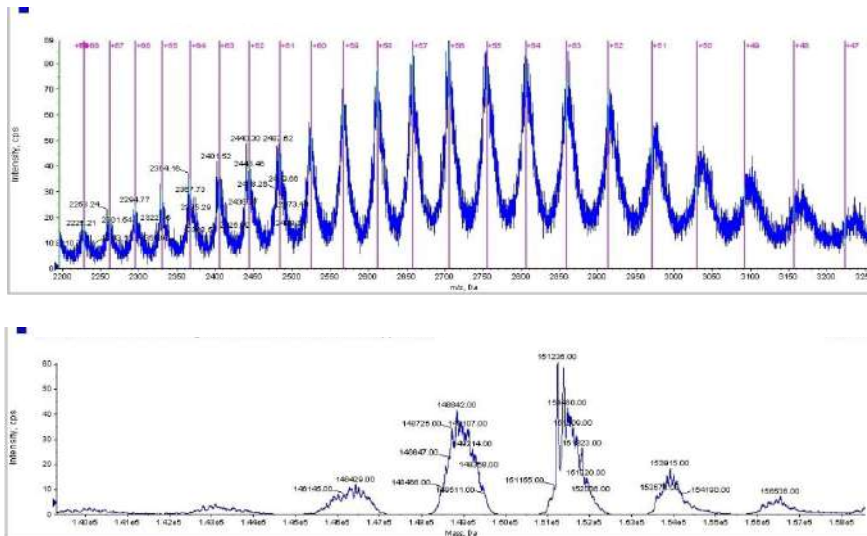
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- Intact mass analysis of complex molecules
- Identification of PEG sites
- Peptide mapping
- Disulphide bridge analysis

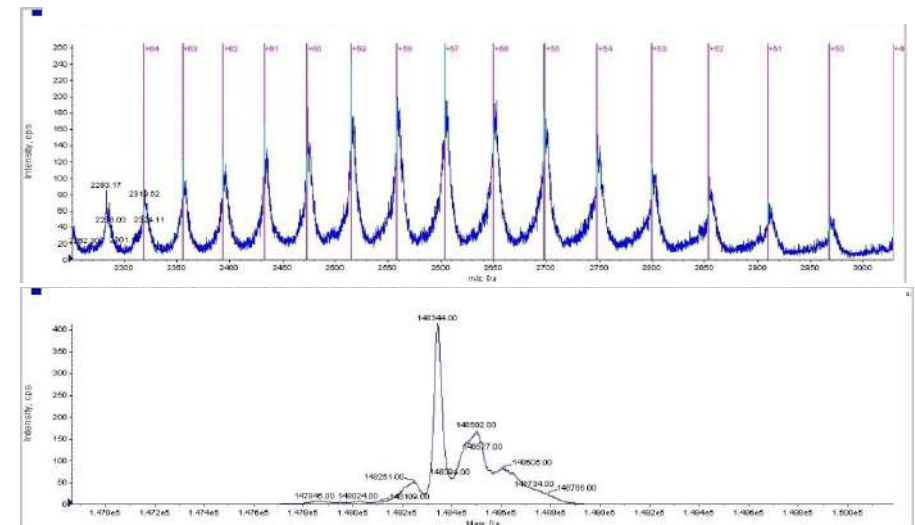


# mAb - Intact mass analysis by ESI-LCMS

Intact (untreated) sample



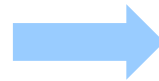
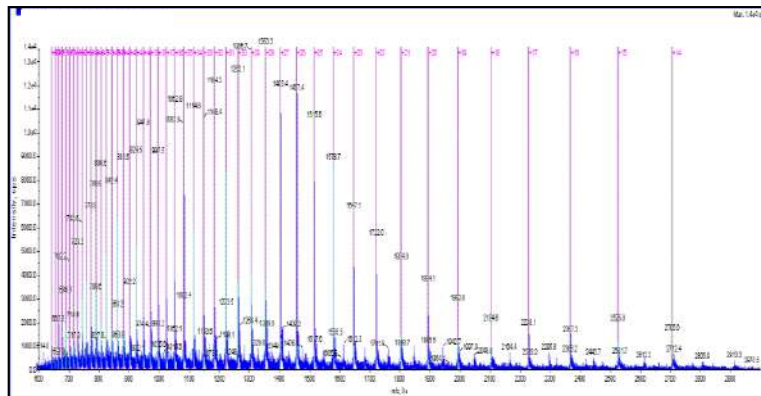
Enzyme (PNGase F) treated sample



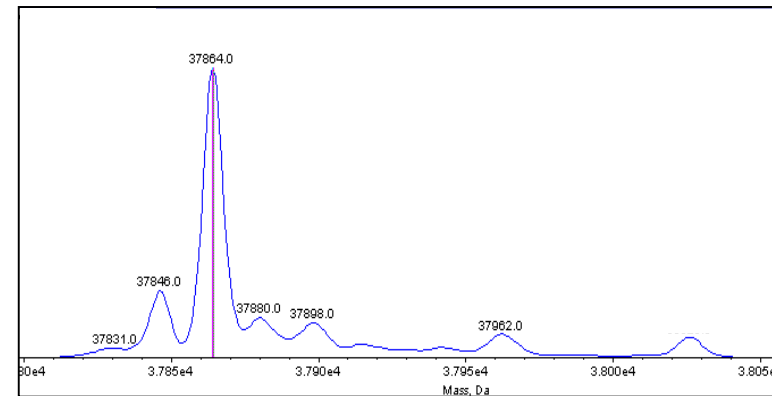
Molecule	Observed Mass (Untreated) [kDa]	Enzyme Treated Mass [kDa]	Difference (intact-enzyme treated)
Intact (whole)	~151	148 344	~ 3,000

# PEGylated proteins - Intact mass analysis by ESI-LCMS (I)

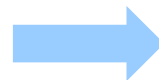
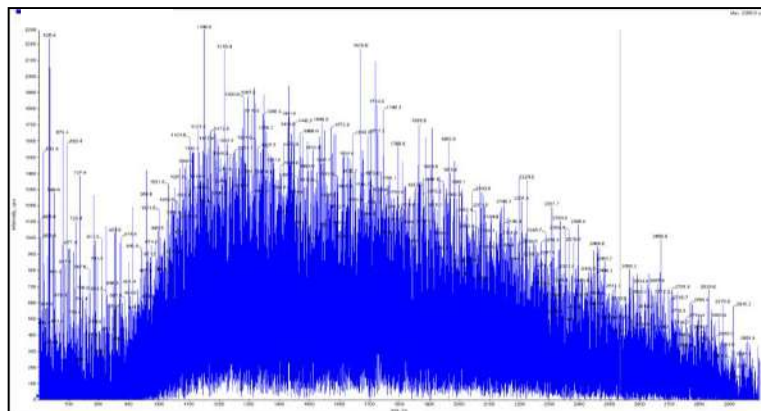
10 µg of Non-PEGylated Control



Protein mass = 37,864 Da



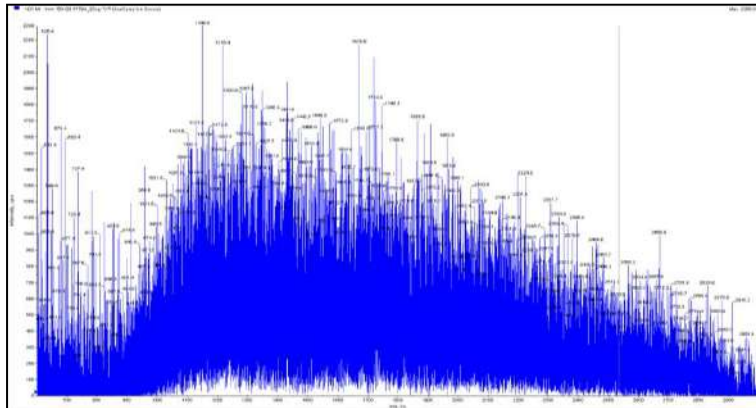
10 µg of PEGylated Protein



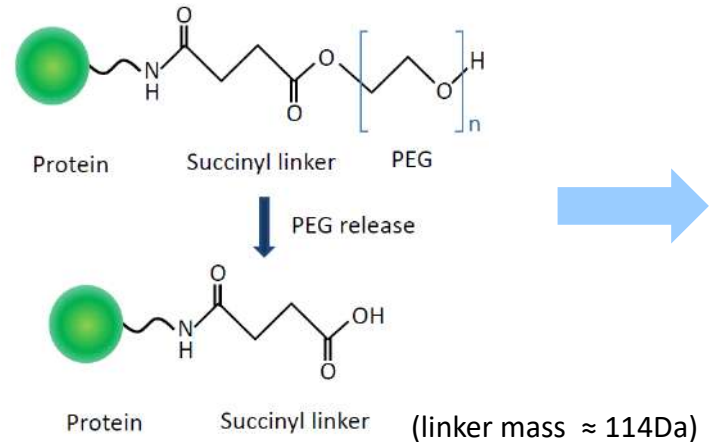
No result

# PEGylated proteins - Intact mass analysis by ESI-LCMS (II)

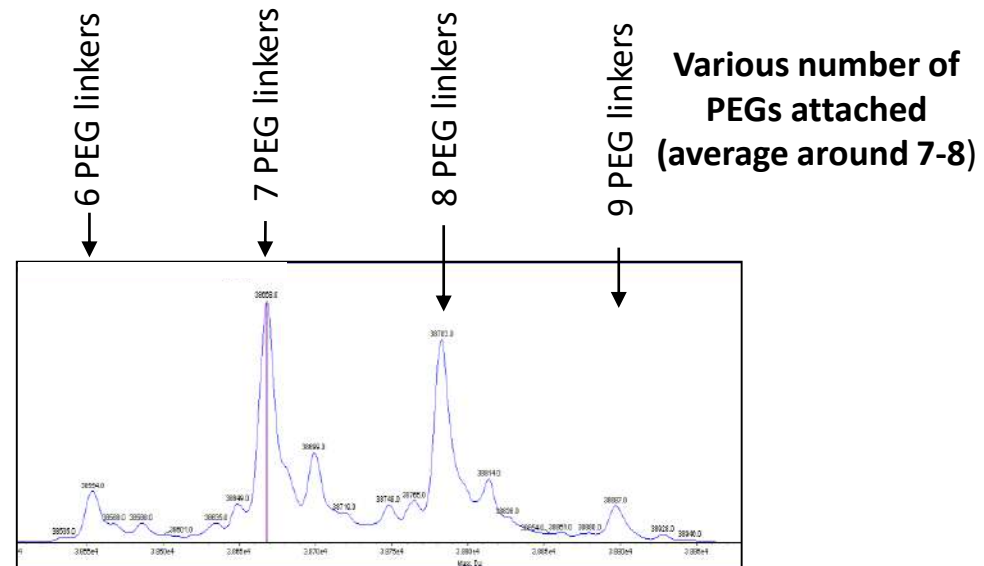
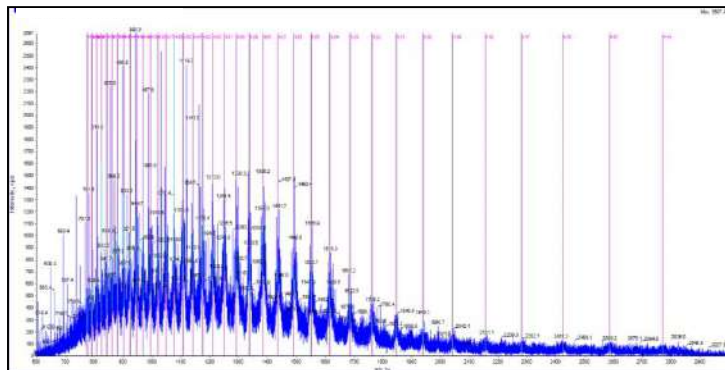
10  $\mu$ g of PEGylated Protein



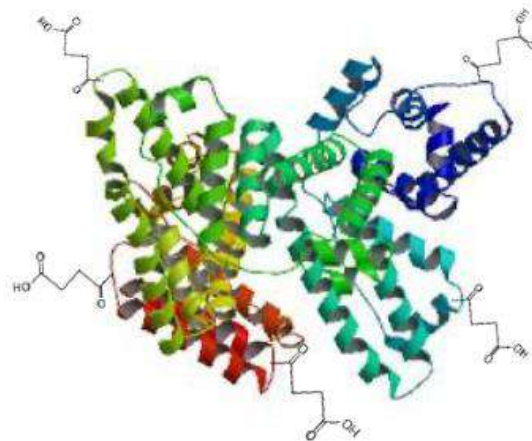
De - PEGylation



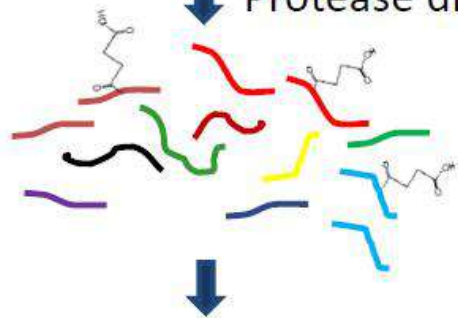
10  $\mu$ g of De-PEGylated Protein



# Identification of PEG linked amino acid residues

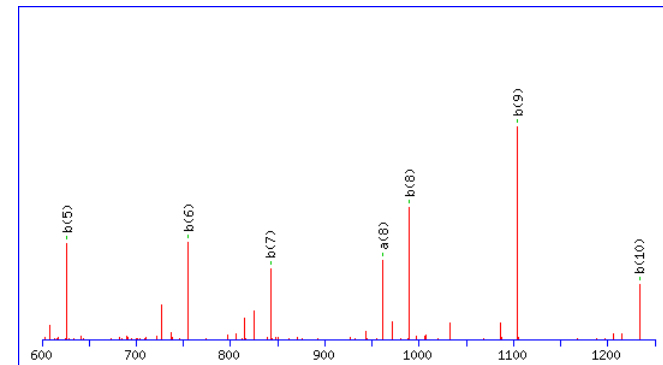


Reduction/alkylation  
Protease digestion



LC-MS/MS

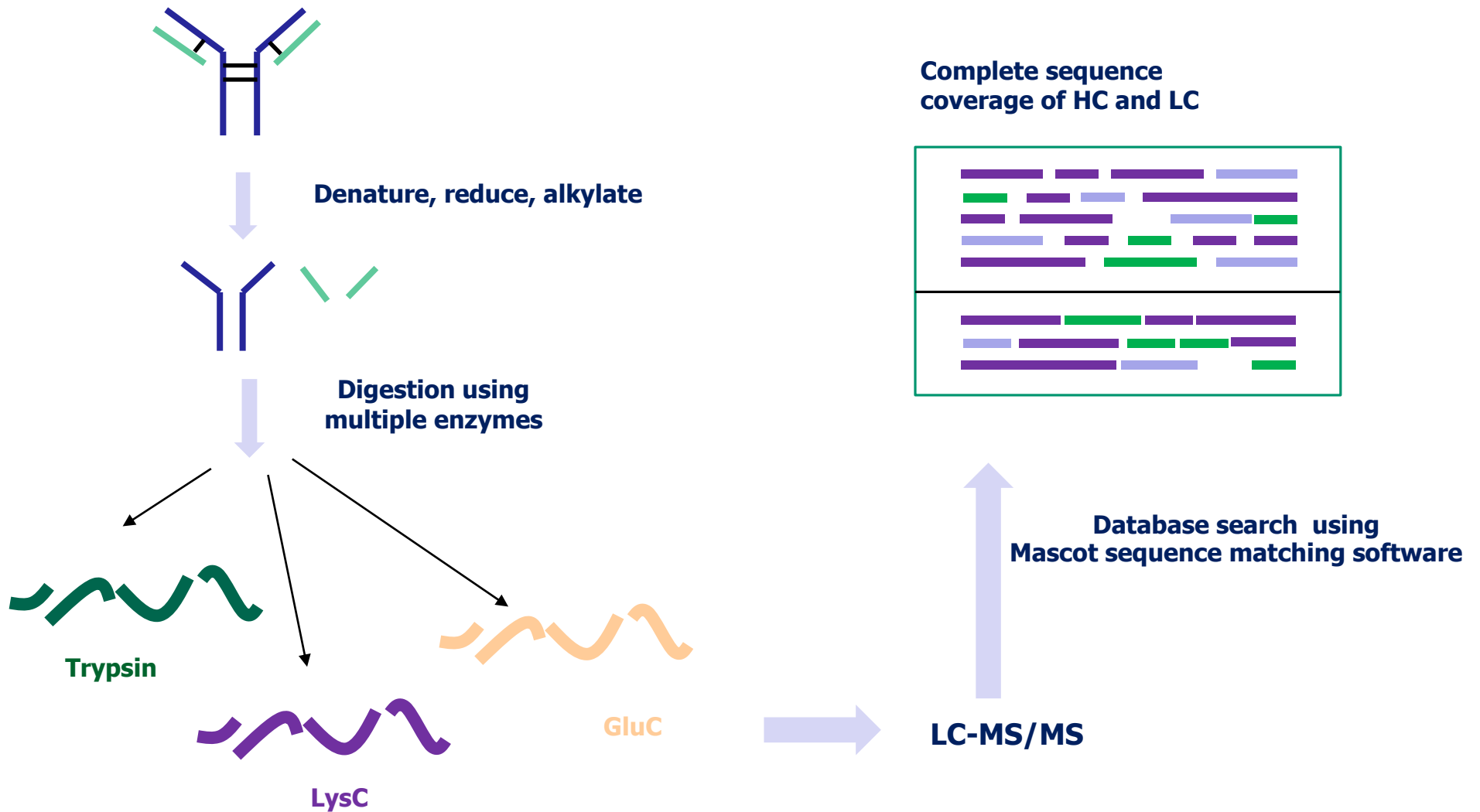
**GRVAK\*ESFDEE**



Filter for high-confident peptides

**Mascot sequence  
matching software**

# Peptide mapping analysis



# Disulphide bridge analysis (I)

## Step 1: Sample preparation

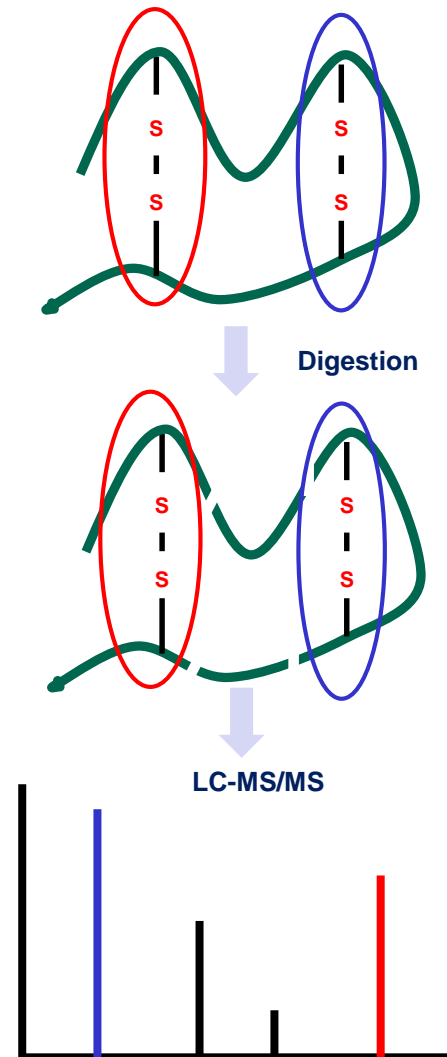
Denatured sample processed under 3 different conditions:

- a) Digested (pH <7)
- b) Alkylated and digested (pH <7)
- c) Reduced, alkylated and digested

## Step 2: LC-MS/MS

### Step 3: Data analysis using

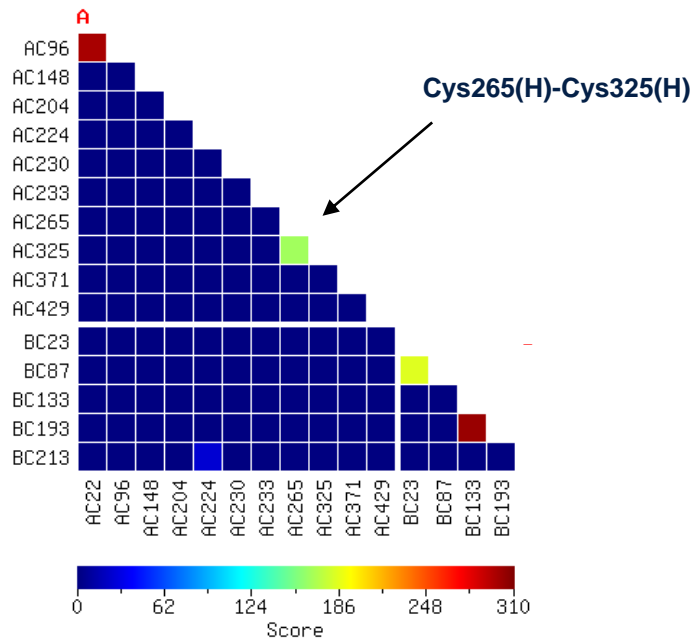
- a) software to automatically assign peptides
- b) manually sequence analysis



# Disulphide bridge analysis (II)

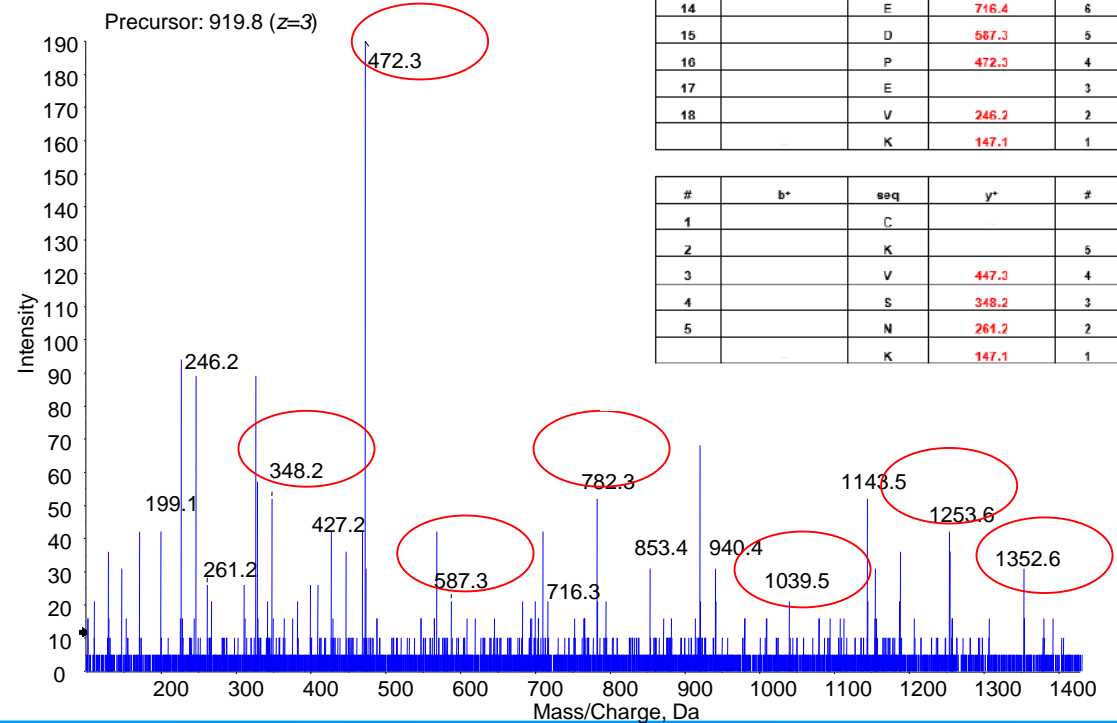
- Software to automatically assign protein disulphide bonds (intra- and inter linked) from mass spectrometry data.

A = Heavy Chain  
B = Light Chain



Scoring profiles show the identified disulphide linked peptides of the antibody

TPEVTCVVVDVSHEDPEVK (Peptide 1)  
|  
CKVSNK (Peptide 2)



#	b*	seq	y*	#
1		T		M
2	199.1	P		18
3	328.2	E		17
4	427.2	V		16
5	528.3	T		15
6	1306.6	C		14
7		V	1451.7	13
8	1504.8	V	1352.7	12
9		V	1253.6	11
10	1718.9	D	1154.5	10
11		V	1039.5	9
12		S	940.4	8
13		H	853.4	7
14		E	716.4	6
15		D	587.3	5
16		P	472.3	4
17		E		3
18		V	246.2	2
		K	147.1	1

#	b*	seq	y*	#
1		C		
2		K		5
3		V	447.3	4
4		S	348.2	3
5		N	261.2	2
		K	147.1	1

# Contact us

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