

Characterization of the Bcl-2 family using structure-aided HMM framework

Valentine RECH DE LAVAL

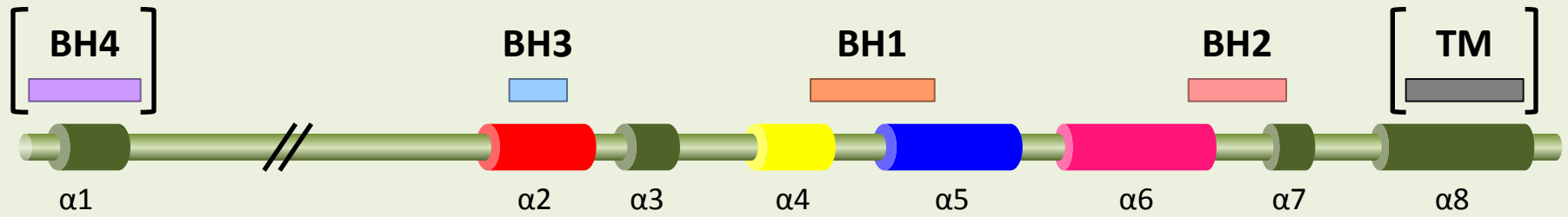
PhD student (first year)

Institut de **B**iologie et **C**himie des **P**rotéines
UMR5086 , CNRS, Université Lyon 1
7, passage du Vercors
69367 Lyon CEDEX 07 - FRANCE

JOBIM 2010, Tuesday 7th September 2010



Bcl-2 family



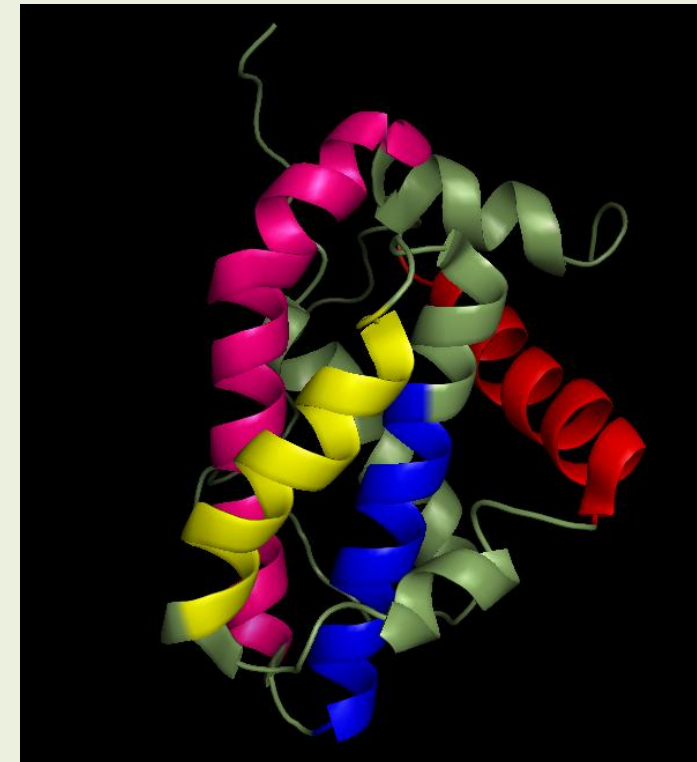
Four-helix bundle (Bcl-2 family core)



Structure and sequence divergent regions

Schematic representation of typical Bcl-2 globular proteins with their Bcl-2 homology (BH) domains ([] represents BH domains not present in all family members)

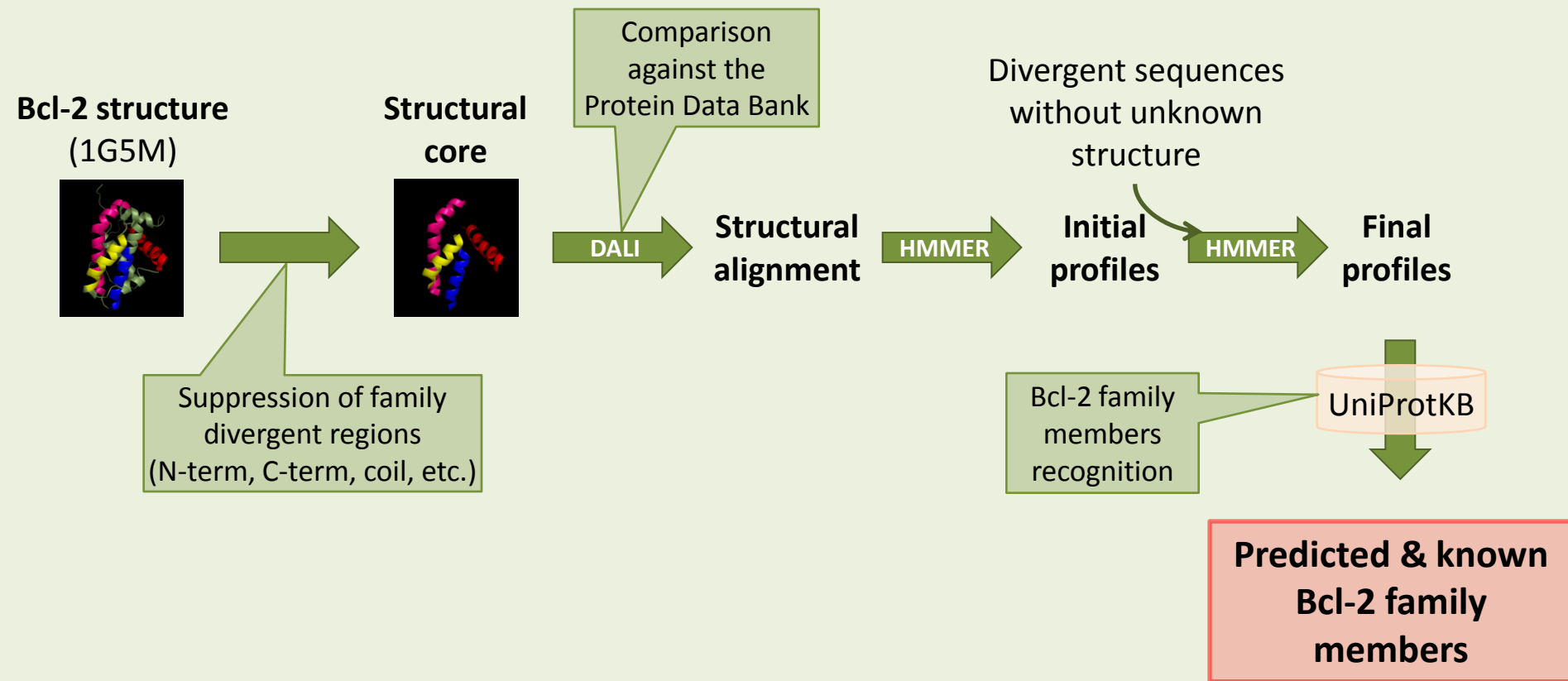
Bcl-2 structure (1G5M)



Objectives

- **Redefine sequence signature** using structure-aided hidden Markov models (HMM) framework.
 - ⇒ To improve automatic identification of family proteins
- Defined groups for profile HMMs are :
 - Cellular : homologous helix-bundled Bcl-2 family members encoded by metazoan genomes
 - Viral : Bcl-2 family members encoded by viral genomes
 - Cellular & Viral : combination of both

Process



Results

- Annotation of viral and cellular members not found by other profiles, *e.g.* putative uncharacterized protein (Acc#:D2H8W0)
=> **15 unflagged proteins, 13 are known Bcl-2 family members**

Output Bcl-2 family members recognition

#ACC	BASE	DR_FLAG	E-VALUE	KINGDOM	ORGANISM	COMMENT
Q5TBC7_2	sp	null	2.8e-37	Metazoa	Homo sapiens (B2L15_HUMAN)	Bcl-2-like protein 15 OS=Homo sapiens GN=BCL2L15 PE=2 SV=1
Q9BZR8_1	sp	BCL-IPR000712	9.8e-29	Metazoa	Homo sapiens (B2L14_HUMAN)	Apoptosis facilitator Bcl-2-like protein 14 OS=Homo sapiens GN=E
Q53F74_1	tr	BCL-IPR000712	9.8e-29	Metazoa	Homo sapiens (Q53F74_HUMAN)	BCL2-like 14 isoform 1 variant (Fragment) OS=Homo sapiens PE
Q3SY13_2	tr	null	2.0e-28	Metazoa	Homo sapiens (Q3SY13_HUMAN)	BCL2-like 12 (Proline rich) OS=Homo sapiens GN=BCL2L12 PE=
Q9HB09_2	sp	BCL-PS01258	2.0e-28	Metazoa	Homo sapiens (B2L12_HUMAN)	Bcl-2-like protein 12 OS=Homo sapiens GN=BCL2L12 PE=1 SV=1
Q2PFL6_1	tr	BCL-IPR000712	9.5e-27	Metazoa	Macaca fasciata (Q2PFL6_MACFA)	Putative uncharacterized protein OS=Macaca fascicularis PE=2 SV
Q4R843_1	tr	BCL-IPR000712	9.5e-27	Metazoa	Macaca fasciata (Q4R843_MACFA)	Testis cDNA clone: QtsA-13490, similar to human BCL2-like 14 (
Q4R3N1_1	tr	BCL-IPR000712	9.5e-27	Metazoa	Macaca fasciata (Q4R3N1_MACFA)	Testis cDNA clone: QtsA-15816, similar to human BCL2-like 14 (
D2H8W0_2	tr	null	1.2e-24	Metazoa	Ailuropoda me (D2H8W0_AILME)	Putative uncharacterized protein (Fragment) OS=Ailuropoda mel
Q0II48_2	sp	null	1.6e-23	Metazoa	Bos taurus (B2L15_BOVIN)	Bcl-2-like protein 15 OS=Bos taurus GN=BCL2L15 PE=2 SV=1
A6QPJ9_2	tr	null	2.2e-22	Metazoa	Bos taurus (A6QPJ9_BOVIN)	BCL2L12 protein OS=Bos taurus GN=BCL2L12 PE=2 SV=1
C6FGJ7_2	tr	BCL-IPR000712	3.2e-22	Metazoa	Bos indicus (C6FGJ7_BOSIN)	Bcl-2 OS=Bos indicus PE=2 SV=1
Q99N36_1	tr	BCL-IPR013279	1.2e-20	Metazoa	Mus musculus (Q99N36_MOUSE)	B-cell leukemia/lymphoma x-gamma (Fragment) OS=Mus musci

ACC = UniProtKB Access

DR_FLAG = InterPro, PROSITE, PFAM, PRINTS, SMART, TIGRFAMs access in UniProtKB flat file of the protein, "null" if any was found.

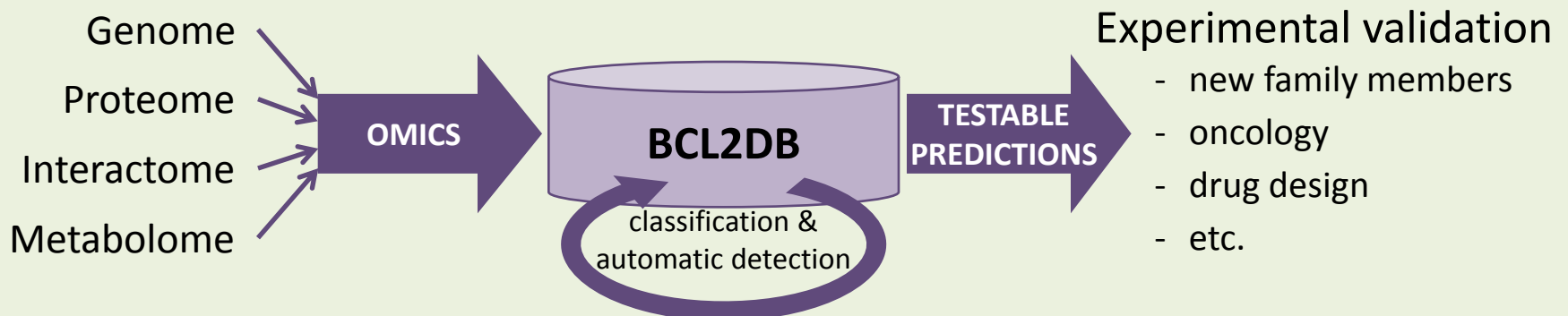
- Discovery of putative candidates for experimental validation at $E > 1.0$, *e.g.* Bcl-WAV (Acc#:D2Y5Q2; $E = 30$; identity with Bcl-2 human = 17.55 %).

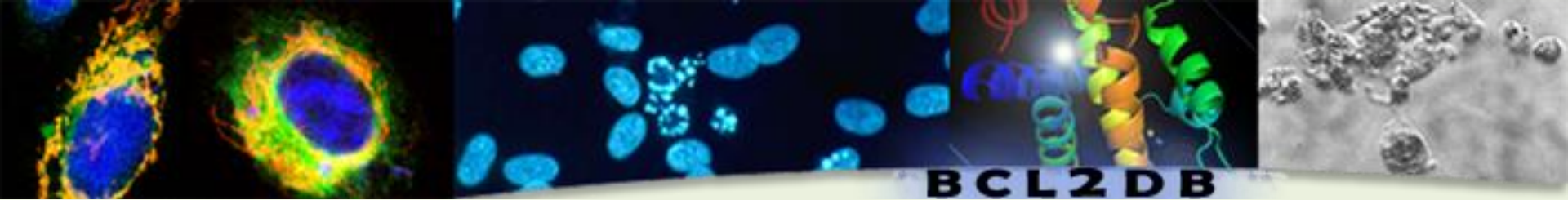
Conclusion

- Improve the functional annotation of massively available sequences.
- Identify potential new Bcl-2 family members

Future work

- Update automatically BCL2DB using defined profiles.
- News profiles to improve homologues and candidates detection again
- **Long term objective : systems biology of apoptosis**





POSTER N° 1

<http://bcl2db.ibcp.fr>

Abdel AOUACHERIA – Valentine RECH DE LAVAL – Gilbert DELÉAGE – Christophe COMBET

Contacts: {a.aouacheria, c.combet, v.rech-de-laval}@ibcp.fr

Juliette HAYER (POSTER N° 69)

Fanny JADEAU (POSTER N° 71)

Paula RAMOS-SILVA (POSTER N° 105)