Curriculum vitae

Josep Vilardell Trench
January 2026

CURRICULUM VITAE

Name: Josep Vilardell Trench
Address: Molecular Biology Institute of Barcelona (IBMB). Baldiri Reixac 10
08028 Barcelona. Tel: +34.93 4020549
email: josep.vilardell@ibmb.csic.es
http://www.ibmb.csic.es/home/jvilardell
http://www.icrea.cat/Web/ScientificStaff/Josep-Vilardell-Trench-517
Date of birth: December 31, 1963
Citizen: Spain

Education

Autonomous University of Barcelona (U.A.B., (Spain).B.S. (Biology)	1986
U.A.B. M.S. in "Biotechnology and Process Development"	1988
U.A.B. Ph. D. in Sciences (Biology: Biochemistry and Molecular Biology)	1990

Professional Experience

NOTE: During the period starting March 2022 to September 2023 I was at MIT, as a visiting scientist in the group of Chris B. Burge, learning to use Computational Biology to address aspects of human pre-mRNA splicing. From October 2023 to July 2025 I took a leave of absence from ICREA for personal reasons.

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Master Degree work; Dept. of Cellular Biology and Physiology, UAB, Spain.	1985 -1987
Graduate Student; Dept. of Molecular Genetics, Centre d'Investigació i Desenvolupament (CSIC), Barcelona, Spain.	1987- 1990
Visiting Fellow; Rhône-Poulenc laboratory (Lyon, France) in Dr. Freyssinet's laboratory.	5 / 1989
Visiting Fellow; Carlsberg Laboratories (Copenhaguen, Denmark) in Dr. John Mundy's laboratory.	9 -12 / 1989
Research Associate; Dept. of Cell Biology, Albert Einstein College of Medicine.	1991 - 1991
Research Fellow; Dept. of Cell Biology, Albert Einstein College of Medicine.	1991 -1993
Research Assistant; Dept. of Cell Biology, Albert Einstein College of Medicine.	1993 -2002
Junior Group Leader; Program of Gene Regulation, Centre de Regulació Genòmica.	2002 - 2010
Visiting Scientist at the group of Chris B. Burge (MIT)	5/2022 - 9/2023
ICREA Research Professor at the IBMB (Including a "leave of absence" from 10/2023 to 7/2025).	2010-present
Scientific director of the IBMB *Genomics Platform*	2025-present

Honors

Scholarship from the Department of Education of the Generalitat de Catalunya.	1986
Predoctoral Fellow of the Spanish Ministry of Science and Education.	1987-1990
CIRIT (Barcelona, Spain) fellowship.	1988-1989
Fellowship from the Spanish Ministry of Science and Education to get training abroad.	1989

FEBS fellowship to attend the "NATO/FEBS Advanced Course on Plant Molecular Biology".	1990
FEBS-J. March fellowship to attend the course "Biochemistry and Genetics of Yeast".	1990
Fulbright Fellow of the Spanish Ministry of Science and Education.	1991-1993
Recipient of the “Ramon y Cajal” award from the Spanish Ministry of Science and Technology	2002-2006
European Community. Marie Curie International Reintegration Grant	2004-2006
Research Group qualified as “Singular” by the Catalan Government AGAUR ref #50	2005
Qualified as an investigator of the “I3" program of the Spanish Ministry of Science to promote the stabilization of junior lab heads	2006
ICREA Professorship (Catalan Institution for Research and Advanced Studies)	2009

Research Grants (as PI)

"Regulation of Gene Expression by RNA-Protein Interactions." Program Ramón y Cajal, Spanish Science Ministry. Own Salary and a small start-up fund	2002-2006
“Metabolisme de l'ARN” Generalitat de Catalunya - DURSI. Ref 2002SGR00175 Juan Valcárcel, Fátima Gebauer, Josep Vilardell (co-PIs) 20,229€	2002-2005
“Regulation of pre-mRNA splicing by the transcript structure and factors that bind it.” Spanish Science Ministry. Ref #BMC2002-00157 124,120€	2003-2005
"RNA Protein Interactions in the Control of Gene Expression". European Community. Marie Curie International Reintegration Grant. Ref. # MIRG-CT-2004-510183 80,000€	2004-2006
“Study of the Molecular Mechanisms of Splicing Regulation in the Model Organism *Saccharomyces cerevisiae*” Spanish Science Ministry. Ref #BFU2005-05215/BMC 105,000€	2006-2008
“Molecular Mechanisms Involved in the Control of pre-mRNA Splicing” Spanish Science Ministry. Ref #BFU2008-00363 170,000€	2009-2011
“Mecanismos Moleculares Responsables del Control del Splicing del pre-mRNA” Spanish Research Council. Ref #200920I195 50,000€	2010
“Molecular Mechanisms of pre-mRNA splicing” Spanish Science Ministry. Ref #BFU2011-25697 204,000€	2012-201

"Control of pre-mRNA splicing and its relevance to disease"
Spanish MINECO (Science Ministry) Ref BFU2014-60550-P
150000€. PI: Josep Vilardell 2015-2018

Virulence Factors in Mycoplasmas. Design of novel antimicrobial therapies. Spanish Science Ministry. Ref PID2021-125632OB-C21
169400€. CoPIs: Ignacio Fita (IBMB) & Josep Vilardell 2022-2023

Publications in peer reviewed journals

Arka Chakraborty, Sébastien Lyonnais, Federica Battistini, Adam Hospital, Giorgio Medici, Rafel Prohens, Modesto Orozco, Josep Vilardell, and Maria Solà
DNA structure directs positioning of the mitochondrial genome packaging protein Abf2p
Nucleic Acids Res **45** (2): 951-967 (2017).

Amit Gautam, Richard J. Grainger, Josep Vilardell, David Barrass and Jean D. Beggs
Cwc21p promotes the second step conformation of the spliceosome and modulates 3' splice site selection.
Nucleic Acids Res. **43**(6):3309-17 (2015).

Antonio de Las Heras-Rubio, Laura Perucho, Rosanna Paciucci, Josep Vilardell, and Matilde Lleonart
Ribosomal proteins as novel players in tumorigenesis
Cancer and Metastasis Reviews **33** (1), 115-141 (2014)

Jorge Pérez-Valle and Josep Vilardell
Intronic features that determine the selection of the 3’ splice site
Wiley Interdisciplinary Reviews WIREs RNA **3,** 707–717 (2012)

Mireya Plass, Carles Codony-Servat, Pedro Gabriel Ferreira, Josep Vilardell, and Eduardo Eyras
RNA secondary structure mediates alternative 3'ss selection in *Saccharomyces cerevisiae*
RNA **18,** 1103–1115 (2012).

Tracy L. Johnson and Josep Vilardell
Regulated pre-mRNA splicing: The Ghostwriter of the Eukaryotic Genome
Biochim. Biophys. Acta **1819**, 538 –545 (2012)

Markus Meyer, Mireya Plass*, Jorge Pérez-Valle*, Eduardo Eyras, and Josep Vilardell
Deciphering 3'ss Selection in the Yeast Genome Reveals an RNA Thermosensor that Mediates Alternative Splicing.
[* *equal contributors*]
Molecular Cell **43** (6), 1033-1039 (2011) (*Science* Editor's Choice Sept. 30).

Bernardo Cuenca-Bono, Varinia García-Molinero, Pau Pascual-García, Hernan Dopazo, Ana Llopis, Josep Vilardell*, and Susana Rodríguez-Navarro*
SUS1 introns are required for efficient mRNA nuclear export in yeast
[* *corresponding authors*]
Nucleic Acids Research **39** (19), 8599-8611 (2011)

Mireia Bragulat, Markus Meyer, Sara Macías, Maria Camats, Mireia Labrador, and Josep Vilardell
RPL30 regulation of splicing reveals distinct roles for Cbp80 in U1 and U2 snRNP cotranscriptional recruitment
RNA **16**, 2033-2041 (2010)
Markus Meyer and Josep Vilardell

"The quest for a message: budding yeast, a model organism to study the control of pre-mRNA splicing"
Briefings in Functional Genomics & Proteomics **8**, 60-67 (2009)

Sara Macías, Mireia Bragulat, Daniel T. Tardiff, and Josep Vilardell
"L30 binds the nascent *RPL30* transcript to repress U2 snRNP recruitment."
Molecular Cell **30**, 732-742 (2008)

Josep Vilardell and Juan Valcárcel
"Powering a two-stroke RNA engine." (News and Views)
Nature Structural Molecular Biology **14**, 574-576 (2007)

Maria M. Konarska, Josep Vilardell and Charles C. Query
"Repositioning of the reaction intermediate within the catalytic center of the spliceosome."
Molecular Cell **21**, 543–553 (2006).
Tao Huang, Josep Vilardell and Charles C. Query
"Pre-spliceosome formation in S.pombe requires a stable complex of SF1-U2AF^{59}-U2AF^{23}"
EMBO J. **21**, 5516-5526 (2002).

Josep Vilardell, Pascal Chartrand, Robert Singer and Jonathan R. Warner.
"The Odyssey of a Regulated Transcript".
RNA **6**, 1773-1780 (2000).

Josep Vilardell, Shaoqing Yu and Jonathan R. Warner.
"Multiple Functions of an Evolutionary Conserved RNA Binding Domain".
Molecular Cell **5**, 761–766 (2000).

Josep Vilardell and Jonathan R. Warner.
"Ribosomal Protein L32 of *Saccharomyces cerevisae* influences both the Splicing of Its Own Transcript and the Processing of rRNA".
Molecular and Cellular Biology **17**, 1959-1965 (1997).

Baojie Li, Josep Vilardell and Jonathan R. Warner.
"An RNA structure involved in feedback regulation of splicing and of translation is critical for biological fitness".
Proceedings of the National Academy of Sciences USA **93**, 1596-1600 (1996).

Hu Li, Seema Dalal, Jennifer Kohler, Josep Vilardell and Susan A. White.
"Characterization of the pre-mRNA binding site for yeast ribosomal protein L32: the importance of a purine-rich internal loop".
Journal of Molecular Biology **250**, 447-459 (1995).

Vilardell, J. and Warner, J.R.
"Regulation of splicing at an intermediate step in the formation of the spliceosome".
Genes & Development **8**, 211-220 (1994).

Vilardell, J., Martínez-Zapater, M., Goday, A., Arenas, C. and Pagès, M.
"Regulation of the rab17 gene pomoter in transgenic Arabidopsis wild-type, ABAdeficient and ABA-insensitive mutants.
Plant Molecular Biology **24**. 561-569 (1994).

Pla, M., Vilardell, J., Guiltinan, M.J., Marcotte, W.R., Niogret, M.F., Quatrano, R.S. and Pagès, M.
"The cis-regulatory element CCACGTGG is involved in ABA and water-stress responses".
Plant Molecular Biology **21**, 259-266 (1993).
Vilardell, J., Mundy, J., Stilling, B., Leroux, B., Pla, M., Freyssinet, G., Pagès, M.

"Regulation of the maize *rab-17* gene promoter in transgenic heterologous systems".
Plant Molecular Biology **17**, 985-993 (1991).

J. Vilardell, A. Goday, M.A. Freire, M. Torrent, C. Martínez, J.M. Torné and M. Pagès.
"Gene sequence, developmental expression and protein phosphorylation of RAB-17 in maize".
Plant Molecular Biology **14**, 423-432 (1990).

Pla. M., Goday, A., Vilardell, J., Gómez, J., Pagès, M.
"Differential regulation of the ABA induced 23-25 Kd proteins in embryos and vegetative tissues of the *viviparous* mutants of maize".
Plant Molecular Biology **13**, 385-394 (1989).

J. Vilardell, M.D. Coll, E. Querol, J. Egozcue.
"Histone electrophoretic pattern in the characterization of synaptonemal complexes".
Cellular and Molecular Biology **35**(2), 207-214 (1989).

Oral Presentations at Scientific Meetings (selected)

J. Vilardell and J.R. Warner
"Ribosomal protein L32 regulates the splicing of its own transcript at an intermediate step of the pliceosome assembly".
Ribosome Synthesis & Nucleolar Function. Cold Spring Harbor, New York, USA. 1994

J. Vilardell and J.R. Warner
"Ribosomal protein L32 regulates the splicing of its own transcript at an intermediate step of the spliceosome assembly".
RNA Processing Meeting of The RNA Society. University of Wisconsin-Madison. 1994

J. Vilardell and J.R. Warner
“A molecular trap in the regulation of splicing?.”
Mid Atlantic Yeast Meeting, Princeton, 1995.

J. Vilardell, S. J. Yu, and J. R. Warner
“Multiple functions for an evolutionarily conserved RNA binding domain.”
Fifth Annual Meeting of the RNA Society, University of Wisconsin, Madison. May 30 - June 4, 2000.

J. Vilardell, S.J. Yu and J.R. Warner
“Conserved RNA-binding for two billion years.”
Yeast Genetics and Molecular Biology Meeting. Seattle 25-30 July. 2000.

M. Konarska, J. Vilardell, and C. Query
“Destabilization of the 5'SS:U6 snRNA helix facilitates the transition from the 1st to 2nd catalytic step of pre-mRNA splicing.”
10th Annual Meeting of the RNA Society. Banff. Canada. May 24-29, 2005.

J. Vilardell
“Saccharomyces cerevisiae as a model to study regulation of splicing.”
Meeting of the Catalan Network of Bioinformatics. Les Avellanes (Spain) 2005. Guest Speaker and Chairman of the Session on Alternative Splicing.

S. Macías, M. Bragulat, D. T. Tardiff, and J. Vilardell
“L30 binds the nascent *RPL30* transcript to repress U2 snRNP recruitment.”
Eukaryotic mRNA processing. Cold Spring Harbor Laboratory, New York. August 22-26, 2007.
J. Vilardell

“Regulation of pre-mRNA splicing.”
6th Meeting on nucleic acids and nucleotides. Research Center “Principe Felipe”, Valencia. November 22-23, 2007. Guest Speaker.

M. Bragulat, S. Macías, J. Vilardell
The Cap-binding protein Cbp80 modulates U2 snRNP recruitment during spliceosome assembly
First International EURASNET Conference on Alternative Splicing. Kraków, Poland, 21-23 May 2008.

M. Meyer, P. San Segundo, D. Barrass, M. Zavolan, J. Beggs, and J. Vilardell.
3' Splice Site Choice in *Saccharomyces cerevisiae*
13th Annual Meeting of the RNA Society, Berlin, July 28th-August 3rd 2008.

Markus Meyer, Mireya Plass, Jorge Pérez-Valle, Eduardo Eyras, and Josep Vilardell
Deciphering 3’ss selection in all yeast introns reveals a thermosensible riboswitch that mediates alternative splicing
Second International EURASNET Conference on Alternative Splicing, Granada, Feb 28 March 3, 2011.

Seminars

"Regulació del splicing en un pas intermig en la formació del spliceosoma". Societat Catalana de Biologia. Centre d’Investigació i Desenvolupament-CSIC, December 1993.

"Ribosomal protein L32 regulates the splicing of its own transcript at an intermediate step of the spliceosome assembly." Rutgers University, New Jersey, Dept. Molecular Biology and Biochemistry, August 1998.

“Regulation of gene expression by controlled spliceosome assembly”. Universitat Pompeu Fabra, Dept. of Biochemistry and Molecular Biology, Barcelona, Spain. March 1999.

"Multiple Steps of Gene Expression Regulated by a Single RNA-Protein Interaction." Albert Einstein College of Medicine. Liver Center. New York. September 27, 2000

_____ Wayne State University. Dept. Biology. Detroit. December 11, 2000.

_____ Catalan Society of Biology. CID-CSIC, Barcelona, Spain. January 2001

_____ University of Pittsburgh. Dept. Biology. Pittsburgh, January 18, 2001.

_____ Georgia Institute of Technology. School of Biology. Atlanta, GA. March 20, 2001.

_____ Wellcome Trust Centre, University of Edinburgh, UK. September 2001

“Regulation of pre-mRNA processing in the yeast *Saccharomyces cerevisiae.*” University Pompeu Fabra, Dept. of Life Sciences. February 24th, 2003.

“Una interacció RNA-proteïna reguladora de l'expressió gènica a múltiples nivells”. University of Barcelona. Dept. of Genetics. PhD Course “Regulació de l'expressió gènica als eucariotes”. March 6th, 2003.

“Regulation of pre-mRNA processing in yeast.” CNRS. Montpellier. France. March 2004

"Multiple Steps of Gene Expression Regulated by a Single RNA-Protein Interaction." University of Barcelona. Oct 2004

“Insights into the control of the spliceosome.” Barcelona Biomedical Research Park. Feb 2008.

“A new strategy to control pre-mRNA splicing.” Institute of Parasitology and Biomedicine López-Neyra. Granada. Spain. Sept. 2008.

“Insights into the control of the spliceosome.” Institute of Molecular Biology of Barcelona. Oct. 2008.

“Yeast as a tool to understand the control of pre-mRNA splicing.” Barcelona Biomedical Research Park. Feb. 2009.

“A reductionist approach to dissect pre-mRNA splicing.” Cancer Epigenetics and Biology Program, PEBC, Barcelona, April 2009.

"Regulated Splicing in Budding Yeast: the Art of Fine Tuning Towards Maximal Competitiveness". Institute of Biochemistry and Microbiology- CSIC. Salamanca (Spain) May 2009.

“Using Yeast to Understand How the Spliceosome Transforms Our Gene Expression”. National Center of Biotechnology (CNB). Madrid, May 2009.

"How alternative splicing can be controled by a thermosensor in the pre-mRNA". University Pompeu Fabra (UPF). Barcelona, October 2011.

“There is more to an intron than meets the eye.” Student invited speaker to the Symposium “Horizons in Molecular Biology”. Bilkent University, Ankara, Turkey. April 2012.

"Pre-mRNA splicing: There is harm in getting the wrong message." Vall d'Hebron Institut de Recerca (VHIR). Barcelona, June 2013. (host Joan Comella)

"Pre-mRNA splicing or the harmony in gene expression." School of Life Sciences and Biotechnology. Shanghai Jiao Tong University. Shanghai, Jul 2013. (host Baojie Li)

“Insights into intron recognition by the core spliceosome.” Wellcome Trust Centre for Cell Biology at the University of Edinburgh. May 2017 (host: Jean Beggs)

Abstracts, Proceedings, and Book Chapters.

Warner, J.R., Vilardell, J., Sohn, J.-H.
“The Economics of Ribosome Biosynthesis In Saccharomyces cerevisiae”
66th Cold Spring Harbor Symposium on Quantitative Biology **66**, pag. 567-574 (2001)
Vilardell, J., Li, B. and Warner, J.R.
"RNA structure and the regulation of splicing".
Nucleic Acid Symposium Series **31**, 275-276 (1994).

Montserrat Pagès, Maria Pla, Josep Vilardell y Adela Goday.
"Water-Stress Responsive Genes in Maize" in *Biotechnology for Aridland Plants*. Mabry, T.J., Nguyen, H.T., Dixon, R.A., Bonness, M.S. Eds. IC^2 Institute. The University of Texas at Austin (1994).

Warner, J.R., Vilardell, J., Morrow, B.E., Ju, Q.D., Eng, F.J., Daveba, M.D. and Alksne, L. "Genetic approaches to the study of eukaryotic ribosomes" in *The Translation Apparatus*. Nierhaus, K.H., Subramanian, A.R., Erdmann, V.A., Franceschi, F. and Wittman-Liebold, B. Eds. Plenum Publishing, New York. pp 109-117 (1993).

Montserrat Pagès, Josep Vilardell, Anders B. Jensen, M. Mar Albà, Margarita Torrent y Adela Goday. "Molecular Biological Responses to Drought in Maize" in *Interacting Stresses on Plants in a Changing Climate*. NATO/ASI Series, Vol I 16. Jackson, M.B., Black, C.R. Eds. Springer-Verlag, Berlin, Heidelberg (1993).

Montserrat Pagès, Dolors Ludevid, Josep Vilardell, M. Angel Freire, Maria Pla, Margarita Torrent and Adela Goday.
"Genes Induced by Abscisic Acid and Water Stress in Maizë in *Plant Molecular Biology* vol 2. Hurrmann R.G. and Larkins, B. Eds. Plenum Press, New York, 1991.

"Isolation and characterization of the synaptonemal complex".
J. Vilardell, M.D. Coll, E. Querol.
Revisiones sobre Biologia Celular (Spanish), **s2**:276, 1987.

Collaborations as referee

- journals:

BBA - Gene Regulatory Mechanisms
Biochemical Journal
EMBO Journal.
FEBS Letters
Journal of Cell Sciences.
Journal of Molecular Biology
Molecular and Cellular Biology.
Nature Comms.
PLoS Genetics
RNA
Nucleic Acids Research

- Editorial Board of Protein and RNA Networks (specialty section of Frontiers in Molecular Biosciences)

- granting agencies:

ANEP (National Agency of Evaluation and Prospectiva). Spain
“Found for Health Research” (FIS) of the Spanish Health Ministry.
Catalan Agency of Managing and Suport for University Research.
FONCYT (Fondo para la Investigación Científica y Tecnológica). Argentina.
Israel Science Foundation
AGAUR
NSF

Supervised PhD Theses

Mireia Bragulat i Bigas
"Estudio de la Regulación del Splicing en *Saccharomyces cerevisiae*: *RPL30* como modelo
Universidad de Barcelona, Facultad de Biología
November 2007

Sara Macías Ribela
"Mechanism of regulation of the *RPL30* pre-mRNA in yeast"
Universitat Pompeu Fabra. Department of Health and Life Sciences
June 2008
Currently a group leader at the School of Biological Sciences, University of Edinburgh.

Markus Meyer
"Cracking the code of 3'ss selection in *S. cerevisiae"*
Universitat Pompeu Fabra. Department of Health and Life Sciences
March 2010

Mireia Labrador Isern
"A Study of Two Distinct Strategies to Control Gene Expression in *Saccharomyces cerevisiae*."
Universitat de Barcelona. Facultad de Biología
March 2015

Teaching

Guest Lecturer in the PhD program "*Life and Health Sciences*" from the University Pompeu Fabra (UPF).	2002-present
Course "Program Based Learning." UPF	2003-2005
Guest Lecturer in the *master* "Cell and Gene Function". UPF.	2004-present
DEA (*Diploma d'estudis avançats*, or Advanced Studies Degree, UPF) panel	2004-present

Participation in Thesis Committees from the UPF, CRG, and IRB (Institute of Biomedical Research of Barcelona).
Member of a number of Thesis Panels.

Other Management Activities

2002-2006:	Organizer of the Weekly Journal Club at the Program of the Gene Regulation at the CRG.
2002- Present:	Inspirer & organizer of the bi-monthly Series Meetings of the Yeast groups of the Area of Barcelona (BYG).
2010-2016:	Organizer of the Weekly Seminar Series of the Departments of Cell Biology & Molecular Genomics. Co-organizer of the IRB/IBMB Barcelona BioMed Weekly Seminar Series.
2025-Present:	Scientific Director of the IBMB *Genomics Platform*

Other Collaborations

2012-2015: Associate Investigator to the RNAREG Consortium, devoted to investigate the role of RNA in disease, particularly in cancer.http://rnareg.maciasnmr.net/index.php?option=com_content&view=article&id=48&Itemid=56&lang=en and http://rnareg.maciasnmr.net/index.php option=com_content&view=article&id=93&Itemid=89&lang=en

2013-2018 Co-organizer of the "Molecular Biology Symposium" of the Catalan Society of Molecular Biology

SABBATICAL (2023)

To a bench scientist it is often difficult to know how and when to apply the computational tools that have become essential to advance in her or his research. To make things more complicated, these tools are being constantly developed. My research plan (outlined below) is motivated by our data that point to a new view for the spliceosome, whereby the "core spliceosome" has capabilities and substrate preferences that have deep implications for alternative splicing. I intend to approach computationally some aspects of these questions, For this I have been fortunate enough to be accepted at the laboratory of Christopher Burge, at MIT, which is an outstanding example of how to combine experimental and in silico data to address biological problems. I am convinced that this constitutes a fantastic opportunity for the development of my research.

Proposed Research:
Control of splicing starts early, with the choice of initial mode of substrate recognition. Thus, instead of just identifying an intron before its removal (recognition by intron definition), many consecutive introns are not spliced as such unless the exon that lies in-between recruits pre-spliceosome components at both ends. This process, therefore, identifies exons before introns (substrate recognition by exon definition). The current model is that exon definition is mediated by special factors that promote spliceosomal interactions across an exon. In their absence, the spliceosome cannot identify the exon, which becomes part of the larger, single intron. A number of characterized splicing events are consistent with this model, leading to the assumption that the spliceosome cannot identify exons without help from additional factors.
To our initial surprise, our data from yeast splicing are challenging this possibility. Yeast splicing machinery is comparatively simple, with few introns and without the many regulatory factors present in other systems. Yet, we have found that the yeast spliceosome is capable of acting in a manner consistent with exon definition, but not consistent with intron definition. Most notably, this exon recognition is affected by mutating any position in the exon. This, excluding specific RNA folding, is in my view totally unexpected.
It is safe to assume that the yeast spliceosome must be close to what could be viewed as "the core" spliceosome, defined as the basal splicing catalyst without specific regulatory factors. That the core spliceosome can identify exons to include them in the mRNA, and that this identification can be altered by the sequence of the exon, have profound consequences to our understanding of splicing. Hence, I propose a detailed examination of substrate recognition by the spliceosome by identifying exons and introns spliced by "exon definition" and by the alternative "intron definition" mechanism. I will study their sequence, structural features, and known splicing requirements. Exons that are alternatively skipped or included are presumably recognized by exon definition, whereas introns that are alternative retained or spliced are likely recognized by intron definition. For constitutively spliced exons and introns, their recognition mode can be deduced from mutations that weaken splice site strength: if they result in exon skipping then exon definition is implicated; if they result in intron retention, then intron definition is implied. Therefore, I will analyze paired genomic/transcriptomic data from Geuvadis, GTEx and other sources to identify such exons and introns, and determine the frequency and conservation of sequence motifs, RNA structures and other features, such as exon and intron length, splice site strength, etc. With these data, I will draw a new model for substrate recognition by the spliceosome, aiming to contribute to our understanding of alternative splicing and its impact on gene expression.