

26<sup>th</sup> Annual

# FSHD International Research Congress

PROGRAM



JUNE 19-20, 2019 | PALAIS DU PHARO | MARSEILLE, FRANCE



## BIENVENUE!

The FSH Society's annual research conference is the premier global platform for the discussion and dissemination of state-of-the-art research on facioscapulohumeral muscular dystrophy (FSHD). Researchers who have networked at this yearly gathering since 1994 have helped to drive fundamental discoveries, with a broad consensus on a "central hypothesis" of the genetic basis of FSHD, development of cellular and animal models, identification of therapeutic targets, and a flowering of ideas for treating FSHD. We are nearing the completion of a Phase 2 clinical trial of a myostatin inhibitor, and the first disease-modifying therapy for FSHD will be launching a Phase 2 trial this year.

The FSH Society's annual research conference is being held for the first time in Europe, to reflect the tremendous contributions of European centers of excellence in FSHD. To keep pace with the expansion of FSHD research, this meeting has grown, too, from one day to two full days. The program committee has particularly reached out to attract clinical researchers, as advancement of drug development brings greater urgency to improving our understanding of the clinical features of FSHD, genotype-phenotype correlations, natural history, and evaluation of disease progression.

With the recent advances in FSHD studies now including large sets of data, greater availability of biomaterials from multiple large research initiatives, and the rapid approach of more clinical trials, the FSHD International Research Congress serves a more important role than ever: to ensure dissemination of the latest ideas and discussion of the field's needs and priorities, combined with collaboration and coordination, to speed up progress toward delivering effective treatments to our patients and families.

We sincerely thank our local host institutions: Marseille Medical Genetics; INSERM; GIPTIS (Genetics Institute for Patients, Therapies, Innovation and Science); the Department of Medical Genetics and Centre de Référence des maladies neuromusculaires et de la SLA, Hôpital de la Timone, Marseille.

We thank you for participating to make such an exciting and dynamic program, and hope that you enjoy the 2019 IRC as much as we have enjoyed planning it.

Sincerely,

### THE 2019 IRC PROGRAM COMMITTEE

June Kinoshita  
ORGANIZATIONAL CHAIR

Frédérique Magdinier  
CO-CHAIR

George Padberg  
CO-CHAIR

Alexandra Belayew

Sabrina Sacconi

Stephen Tapscott

Rabi Tawil

Rossella Tupler

Peter Zammit



## MICHEL FARDEAU

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Professor Fardeau is emeritus research director at the Centre national de la recherche scientifique (CNRS) and honorary professor at the CNAM. In 1977, as a young research director, Prof. Fardeau became head of the biology and neuromuscular pathology unit at CNRS, which he directed until 1996. Initially a small team, four people established the first unit working specifically in the field of muscle diseases: the electron microscopy department at La Salpêtrière. The team grew gradually, to the point that it moved from La Salpêtrière to Fer à Moulin, and then it became necessary to build the Institute of Myology, with a staff that now exceeds several hundred members, which Prof. Fardeau served as medical and scientific director until his retirement in 2006. Prof. Fardeau has received numerous awards and international recognition for his work. In 2015, Prof. Fardeau received the Grand Medal of the French National Academy of Medicine. He was honored for his outstanding career that has been entirely devoted to the biology and pathology of muscle. He is currently a member of the scientific council of the Association Française contre les Myopathies.



## BRADLEY R. CAIRNS

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Dr. Cairns received his B.S. (Honors) in chemistry from Lewis and Clark College in 1987. He received his PhD in cell biology in 1996 from Stanford University, where he worked with Nobel Laureate Roger Kornberg on signal transduction and chromatin remodeling. Dr. Cairns received formal postdoctoral training with Fred Winston, PhD, in the Department of Genetics at Harvard Medical School (funding from the Leukemia Society of America), where Dr. Cairns continued to study chromatin remodeling complexes. In 1998, he joined the faculty of the Department of Oncological Sciences at the University of Utah School of Medicine. In 2000, he was appointed as an investigator with the Howard Hughes Medical Institute. He is currently professor and chair of the Department of Oncological Sciences, and is the Jon and Karen Huntsman Presidential Professor in Cancer Research and senior director of basic science at the Huntsman Cancer Institute. He is co-leader of the Nuclear Control of Cell Growth and Differentiation Program. He was elected to the American Academy of Arts and Sciences in 2017. The Cairns lab strives to understand chromatin-transcription relationships – with an emphasis on development and cancer – and effectively utilizes biochemistry, genetics, and genomics in multiple model systems.





# SCHEDULE DAY 1

PALAIS DU PHARO, SALLE DE LA MAJOR

**7:30–8:30**

## REGISTRATION

Please take breakfast at your hotel before coming to the Palais du Pharo.

**8:30–8:35**

## WELCOME

Mark Stone, president & CEO, FSH Society  
George Padberg & Frédérique Magdinier, co-chairs

**8:35–9:00**

## PLENARY: FSHD, the patients' perspective

**9:00–9:20**

## KEYNOTE: A historical perspective on FSHD

Michel Fardeau, Institute of Myology

**9:20–9:30**

## KEYNOTE: FSHD genetics today

Nicholas Levy, Medical Genetics, Aix-Marseille Université

**9:30–9:45**

## Report on the March 2019 Industry Collaborative Workshop on FSHD Therapeutics

Jamshid Arjomand, chief science officer, FSH Society

**9:45–10:10**

## COFFEE BREAK

Break sponsor: Genomic Vision

**10:10–11:10**

## PLATFORM SESSION 1

### The FSHD clinical phenotype

Chair, George Padberg; co-moderator, Peter Lunt

**10:10–10:25**

1.1 Clinical characteristics of childhood FSHD; implications for trial-readiness.

Nicol Voermans (presenter), RJM Goselink

**10:25–10:40**

1.2 Clinical examination of scapula function in patients with FSHD.

Jos IJspeert

**10:40–10:55**

1.3 Facioscapulohumeral muscular dystrophy (FSHD) has a talk with endocrinologic parameters: estradiol, progesterone and testosterone.

Ceren Hangül

**10:55–11:10**

1.4 High frequency of keratinocyte-related skin diseases in FSHD.

Sabrina Sacconi (presenter), Luisa Villa

**11:10–12:10**

## PLATFORM SESSION 2

### Genetics and molecular findings for genotype-phenotype correlations and genetic diagnostics

Chair, Rossella Tupler; co-moderator, Meena Upadhyaya

**11:10–11:25**

2.1 Large scale genotype-phenotype correlation study in 1,703 carriers of D4Z4 reduced alleles from the Italian National Register for FSHD.

Fabiano Mele

**11:25–11:40**

2.2 Exploring the pathogenicity of DUX4 permissive and non-permissive 4qA haplotypes in FSHD.

Muriel Kuipers

**11:40–11:55**

2.3 SMCHD1 mutation spectrum for facioscapulohumeral muscular dystrophy type 2 (FSHD2) and Bosma arhinia microphthalmia syndrome (BAMS) reveals disease-specific localization of variants in the ATPase domain.

Richard Lemmers

**11:55–12:10**

2.4 Trans-generational effects in FSHD: clinical and lab evidence for imprinting, possibly cumulative?

Peter Lunt

**12:10–13:15**

## LUNCH: PHAR CLUB

Lunch sponsor: Muscular Dystrophy Association

**13:15–15:15**

## PLATFORM SESSION 3

### Molecular mechanisms: DUX4, downstream targets, other players

Chair, Pete Zammit; co-moderator, Michael Kyba

**13:15–13:30**

3.1 Consequences of DUX4 expression in vitro and in vivo.

Stephen Tapscott (presenter), Rebecca Resnick



# SCHEDULE DAY 1

PALAIS DU PHARO, SALLE DE LA MAJOR

## 13:30–13:45

3.2 Single-cell transcriptomes of myogenic cells in facioscapulohumeral muscular dystrophy.  
*Laurence Hayward (presenter), Dongsheng Guo*

## 13:45–14:00

3.3 Generation of an iPSC model of FSHD and unveiled aspects of DUX4 expression under genotoxic stresses.  
*Mitsuru Sasaki-Honda*

## 14:00–14:15

3.4 In vitro challenging of facioscapulohumeral muscular dystrophy macrophages derived monocytes: the role of trained innate immunity in FSHD.  
*Anna Greco*

## 14:15–14:30

3.5 The interplay between myogenesis and inflammation in FSHD.  
*Maryna Panamarova*

## 14:30–14:45

3.6 Identification of the hyaluronic acid pathway as a novel therapeutic target for facioscapulohumeral muscular dystrophy.  
*Alec M DeSimone*

## 14:45–15:00

3.7 The role of mitochondrial reactive oxygen species in pathology of FSHD myogenesis.  
*Anna Karpukhina*

## 15:00–15:15

3.8 Identification of the DUX4-targeted miRNome from a library of 1,881 natural human miRNAs.  
*Nizar Y Saad*

## 15:15–15:30

### COFFEE BREAK

Break sponsor: University of Nevada, Reno

## 15:30–17:00

### PLATFORM SESSION 4

#### Molecular mechanisms and animal models

Chair, *Alexandra Belayew*; co-moderator, *Scott Harper*

## 15:30–15:43

4.1 Transgenic mice expressing tunable levels of DUX4 develop characteristic facioscapulohumeral muscular dystrophy-like pathophysiology ranging in severity.  
*Peter Jones (presenter), Takako Jones*

## 15:43–15:56

4.2 Muscle xenografts reproduce key molecular features of FSHD.  
*Robert Bloch*

## 15:56–16:09

4.3 Clinically advanced p38 inhibitors suppress DUX4 expression in cellular and animal models of FSHD.  
*Fran Sverdrup (presenter), Jonathan Oliva*

## 16:09–16:22

4.4 Examining the etiology of myopathy mediated by the transcription factor Dux.  
*Paul Gregorevic (presenter), Kevin I Watt*

## 16:22–16:35

4.5 Cellular pathway disruptions in mouse muscle expressing low levels of DUX4 protein.  
*Joel R Chamberlain (presenter), Maya Zavaljevski*

## 16:35–16:48

4.6 Study of regenerative potential of human perivascular cells expressing DUX4.  
*Fabiola Moretti (presenter), Silvia Maiullari*

## 16:48–17:00

4.7 Retrotransposon-mediated repression of Dux in early mouse development.  
*Michelle Percharde*

## 17:00–18:00

### BREAK

## 18:00–20:00

### POSTER SESSION

Grand Large (1st level)

## 19:00–20:00

### COCKTAILS

Eugenie Ballroom (ground level)

## 20:00–22:30

### CONFERENCE BANQUET

Eugenie Ballroom, Palais du Pharo



# SCHEDULE DAY 2

PALAIS DU PHARO, SALLE DE LA MAJOR

**8:25–8:30**

## WELCOME

Please take breakfast at your hotel before coming to the Palais du Pharo.

*George Padberg & Frédérique Magdinier, co-chairs*

**8:30–9:15**

## KEYNOTE: The role of DUX4 in development

*Brad Cairns, University of Utah*

**9:15–10:15**

## PLATFORM SESSION 5

### DNA methylation and epigenetics

*Chair Frédérique Magdinier; co-moderator, Marnie Blewitt*

**9:15–9:27**

5.1 The crystal structure of SMCHD1's hinge domain and the pathway for SMCHD1 chromatin association reveal a model for how SMCHD1 is targeted to chromatin.

*Marnie Blewitt/Kelan Chen*

**9:27–9:39**

5.2 Methylation of the region distal to the D4Z4 array is lower than predicted in FSHD1.

*Giancarlo Deidda (presenter), Patrizia Calandra*

**9:39–9:51**

5.3 Identification of a new epigenetic factor required for the aberrant expression of DUX4 in FSHD muscular dystrophy.

*Davide Gabellini (presenter), Roberto Giambruno*

**9:51–10:03**

5.4 The D4Z4 macrosatellite sequence as a prototype element for formation of long distance loops: implication in pathologies.

*Jerome D Robin (presenter), Marie-Cécile Gaillard*

**10:03–10:15**

5.5 Apabetalone, a CVD phase 3 clinical-stage BET inhibitor, opposes DUX4 expression in primary human FSHD muscle cells.

*Christopher D Sarsons*

**10:15–10:30**

## COFFEE BREAK

*Break sponsor: Filnemus*

**10:30–11:30**

## PLATFORM SESSION 6

### Muscle pathology and imaging

*Chair, Rabi Tawil; co-moderator, Giorgio Tasca*

**10:30–10:45**

6.1 Membrane repair deficits in facioscapulohumeral muscular dystrophy.

*Yi-wen Chen (presenter), Sreetama Sen Chandra*

**10:45–11:00**

6.2 Muscle ultrasound is a responsive biomarker in FSHD.

*Baziel van Engelen (presenter), Rianne JM Goselink*

**11:00–11:15**

6.3 Long-term follow-up of MRI changes in thigh muscles of patients with facioscapulohumeral dystrophy: a quantitative study.

*Emmanuelle Salort-Campana*

**11:15–11:30**

6.4 PATCHS MRI score correlates with clinical severity in facioscapulohumeral muscular dystrophy.

*Wenhua Zhu (presenter), Yiqi Liu*

**11:30–12:15**

## PLATFORM SESSION 7

### Natural history

*Chair, Sabrina Sacconi; Co-moderator, Karlien Mul*

**11:30–11:45**

7.1 Clinical categories to describe the phenotypic complexity associated with D4Z4 reduced allele.

*Giulia Ricci*

**11:45–12:00**

7.2 Differentiating phenotypes in carriers of 7–8 D4Z4 reduced alleles: experience of the Italian National Registry for FSHD.

*Lucia Ruggiero*

**12:00–12:15**

7.3 Longitudinal MRI evaluation of muscle involvement in FSHD.

*Mauro Monforte*



# SCHEDULE DAY 2

PALAIS DU PHARO, SALLE DE LA MAJOR

**12:15–12:45**

## PLATFORM SESSION 8

### Registries

*Chair, Sabrina Sacconi*

**12:15–12:45**

8.1 Report on national FSHD registries.

*Karlien Mul*

**12:45–14:30**

## LUNCH BREAK & POSTER SESSION: PHAR CLUB

*Lunch sponsor: National Institutes of Health*

**14:30–16:00**

## PLATFORM SESSION 9

### Therapeutic interventions

*Chair, Stephen J. Tapscott; co-moderator, Fran Sverdrup*

**14:30–14:45**

9.1 Dose escalation results from a phase 2 study of ACE-083, a local muscle therapeutic, in patients with facioscapulohumeral muscular dystrophy (FSHD).

*Jeffrey M Statland*

**14:45–15:00**

9.2 The discovery of a drug target and development candidate that inhibits the expression of DUX4, the root cause of FSHD.

*Owen B Wallace*

**15:00–15:15**

9.3 Translating DUX4-targeted RNAi-based gene therapy for FSHD.

*Lindsay Wallace*

**15:15–15:30**

9.4 Inhibition of DUX4 expression with antisense gapmers as a therapy for facioscapulohumeral muscular dystrophy.

*Rika Maruyama*

**15:30–15:45**

9.5 Targeting the DUX4 transcriptional mechanism of action.

*Michael Kyba (presenter), Darko Bosnakovski*

**15:45–16:00**

9.6 Discovery of novel small molecule treatment options for FSHD.

*Joris De Maeyer (presenter), Geese Marcus*

**16:00–16:15**

## COFFEE BREAK

*Break sponsor: Muscular Dystrophy UK*

**16:15–17:15**

## PLATFORM SESSION 10

### Clinical evaluation, outcome measures, clinical trial readiness (4 talks, 60 minutes)

*Chair, Jeffrey Statland; co-moderator, Baziel van Engelen*

**16:15–16:30**

10.1 Conceptual framework for measurement of treatment effect on DUX4 in losmapimod phase 2 trials.

*Lucienne Ronco*

**16:30–16:45**

10.2 Elucidating the extent and pattern of longitudinal upper extremity reachability decline in FSHD, using Kinect sensor-based reachable workspace outcome measure.

*Jay Han*

**16:45–17:00**

10.3 Development of an optimized Timed-Up-and-Go Test for the FSHD population.

*Maya N Hatch*

**17:00–17:15**

10.4 The facioscapulohumeral muscular dystrophy specific Rasch-built Overall Disability Scale (FSHD-RODS).

*Karlien Mul*

**17:15–18:00**

## MEETING CONCLUSION & PRIORITIES DISCUSSION

**18:00**

## ADJOURN



## POSTER SESSIONS

### PALACE DU PHARO, GRAND LARGE (1st level)

Odd-numbered posters on July 19, 18:00-20:00

Even-numbered posters on July 20, 12:45-14:30

### POSTER NUMBER

### ABSTRACT TITLE, PRESENTING AUTHOR/FIRST AUTHOR (if different from presenting)

- |    |  |
|----|--|
| 1  | Modelling FSHD by cell transplantation and genetic manipulation in a zebrafish model.<br><i>Camilla Farnetani</i>  |
| 2  | The role of estrogen receptor related beta (ESRR $\beta$ ) in FSHD-1 mechanism.<br><i>Anna Pakula</i>  |
| 3  | U7-snRNA-Mediated Exon Skipping of the Toxic DUX4 Gene as a Promising Therapeutic Approach for Facioscapulohumeral Muscular Dystrophy. (Corrected.)<br><i>Afroz Rashnonejad</i>                        |
| 4  | The RNA binding protein FRG1 controls transcription landscape regulating muscle maturation and metabolism.<br><i>Antonio Vallarola</i>   |
| 5  | Circulating biomarkers for facioscapulohumeral muscular dystrophy.<br><i>Yi-Wen Chen, Christopher R Heier</i>  |
| 6  | Measurement properties of performance-based outcome measures of physical functioning in individuals with facioscapulohumeral dystrophy (FSHD) - A systematic review.<br><i>Katy de Valle</i>           |
| 7  | Process Abstract: Implementing Kinect sensor-based reachable workspace (RWS) measurement system in a multi-site, international FSHD clinical study.<br><i>Jay Han</i>                                  |
| 8  | Proposal of a neuropsychological protocol to study cognitive functions in FSHD.<br><i>Elisa Lai</i>  |
| 9  | Self-report questionnaire vs. clinical evaluation form in the French National Registry on facioscapulohumeral dystrophy: a statistical comparison.<br><i>Benoit Sanson</i>                             |
| 10 | Patterns of muscle involvement, predictive characteristics, and meaningful change for functional motor tasks in FSHD.<br><i>Jeffrey M Statland</i>   |
| 11 | Biomarker identification by high-resolution proteomic approach in FSHD.<br><i>Giorgio Tasca, Victor Corasolla Carregari</i>  |
| 12 | Effect of Creatine Monohydrate on Functional Muscle Strength and Muscle Mass in Children with FSHD: a Multi-Centre, Randomised, Double-Blind Placebo-Controlled Crossover Trial<br><i>Ian Woodcock</i> |
| 13 | Phenotype may predict the clinical severity of facioscapulohumeral muscular dystrophy.<br><i>Wenhua Zhu, Yiqi Liu</i>  |
| 14 | An in situ hybridization-based method for detecting DUX4 RNA expression in vitro.<br><i>Amini Chermahini-Gholamhossein</i>   |
| 15 | Characterization of human perivascular cells as a new cellular model of facioscapulohumeral muscular dystrophy.<br><i>Giorgia di Blasio</i>  |
| 16 | Investigation of the effect of estrogen on DUX4/ $\beta$ -catenin/PAX3-7 protein levels in facioscapulohumeral muscular dystrophy (FSHD).<br><i>Ceren Hangül</i>                                       |
| 17 | Single-cell transcriptomics reveals DUX4 expression during early stages of myogenesis in FSHD1.<br><i>Oliver King, Anna Pakula</i>   |





## POSTER SESSIONS

**PALACE DU PHARO, GRAND LARGE (1st level)**

Odd-numbered posters on July 19, 18:00-20:00

Even-numbered posters on July 20, 12:45-14:30

### POSTER NUMBER

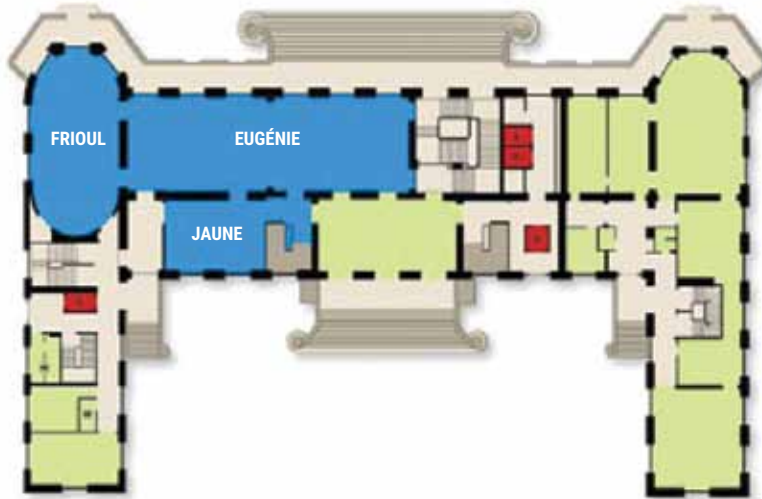
### ABSTRACT TITLE, PRESENTING AUTHOR/FIRST AUTHOR (if different from presenting)

- 18** Exploring the relationship between DUX4 and hypoxia-inducible factor (HIF1 $\alpha$ ).  
*Thuy-Hang Nguyen*
- 19** DUX4 is a co-repressor of the progesterone and glucocorticoid nuclear hormone receptor.  
*Alberto Luis Rosa, Julieta Quintero*
- 20** Deciphering the mechanism of herpesviral DUX4 induction.  
*Stephanie Walter*
- 21** Genetic and epigenetic analysis of the FSHD-linked 4q35 region in rare female "Coats' disease" patients.  
*Robin Fitzsimons*
- 22** SMCHD1 plays a pleiotropic role in euchromatin or heterochromatin regulation with consequences in rare diseases.  
*Camille Laberthonnière, Camille Dion*
- 23** NO66 acts together with SMCHD1 as a co-repressor of DUX4 in facioscapulohumeral muscular dystrophy (FSHD).  
*Mara Tihaya*
- 24** Do different phenotypes predict the clinical course of FSHD?  
*Giulia Ricci*
- 25** An innate immunity model of FSHD muscle pathology.  
*Katelyn Daman*
- 26** Elucidating the role of metabolic stress and mitochondrial dysfunction in FSHD.  
*Philipp Heher*
- 27** Intramuscular pattern of fat infiltration measured by MRI to identify disease initiation in FSHD.  
*Linda Heskamp*
- 28** The French National Registry of patients with facioscapulohumeral muscular dystrophy.  
*Céline Guien*
- 29** An update on the UK FSHD Patient Registry in 2019 and future considerations.  
*Ben Cody Porter*
- 30** Safety and tolerability of losmapimod, a selective p38/MAPK inhibitor, for treatment of FSHD at its root cause.  
*Diego Cadavid*
- 31** Antisense therapy for facioscapulohumeral muscular dystrophy.  
*Yi-Wen Chen, Aiping Zhang*
- 32** Phase 1 clinical trial of losmapimod in FSHD.  
*Michelle L Mellion*
- 33** Losmapimod reduces DUX4 expression across FSHD patient-derived myotube cells.  
*Alejandro Rojas*
- 34** MyoScreen™, a drug discovery platform for FSH muscular dystrophy.  
*Joanne Young*
- 35** Single-nucleus RNA-seq identifies divergent populations of FSHD2 myotube nuclei.  
*Katherine Williams, Shan Jiang*

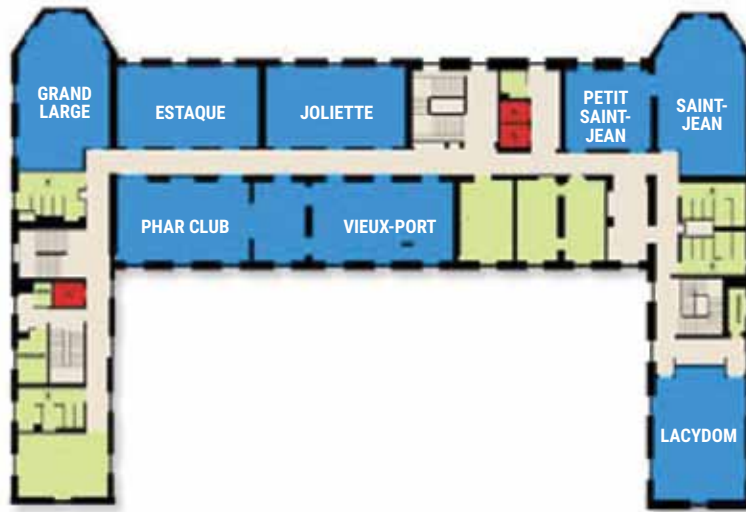


# FLOOR MAPS

**GROUND LEVEL**



**FIRST LEVEL**



**SECOND LEVEL**



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