The Action Duchenne 14th International Annual Conference

11 & 12 November 2016

The Hilton London Metropole

225 Edgware Road London W2 1JU

Welcome to the Action Duchenne International Conference 2016

A word from our CEO

I joined Action Duchenne over five years ago after meeting Nick Catlin, Janet Hoskin and Angela Stringer, who inspired me to make a difference. From the outset, myself and the team learnt the most from the families and young people; being privileged to listen to their stories, supporting them in any way we could. I relished the fundraising, advocacy and campaigning, everyday seeing how we helped.

I soon got more involved in research and a lot has changed; a few minor setbacks along the way but many more advances and a palpable sense of hope. This summer, after a long and hard fought campaign by our families and other key stakeholders; NICE and NHS England made a landmark decision for managed access of translarna treatment for those eligible and with nonsense mutations.

Whilst things are moving at such an incredible pace, Action Duchenne's approach hasn't changed, we always aim to think of everyone and do as much as we can; the newly diagnosed families, those with young children, pre-teens (boys and girls), teenagers, adults, but also their family members.

The international conference encapsulates what we do best as a community and what we have achieved both in the UK and internationally with Action Duchenne at the forefront; to inform, inspire, collaborate and support each other. Thank you for your presence, contributions and for spurring us on to do better. We truly hope you have a productive and enjoyable weekend.

Diana Ribeiro, CEO Action Duchenne

The campaign for Translarna

My son Thomas enrolled on the PTC020 trial for Translarna in 2013 having only just missed out on one of the earlier trials in 2007 due to being too young at the time. The subsequent campaign to get Translarna prescribed on the NHS in England has been both protracted and infuriating but one which has finally yielded a positive outcome. My personal involvement has included speaking to MPs at Westminster, writing to NICE and even producing a series of stop motion lego movies on youtube to highlight the failings of the regulatory processes for assessing drugs for rare conditions. Google 'DMD Moviemaker' to view them! I can also remember reading through 620 pages of NICE committee reports on a family trip to America and being sufficiently alarmed to prepare an individual response to NICE as well as contributing to Action Duchenne's comprehensive submission. Securing access to Translarna under the Managed Access Agreement is a huge achievement for the Duchenne community and means that there are now appropriate regulatory processes in place for the other Duchenne treatments coming forward. A great deal of credit and thanks must be given to Action Duchenne and our dedicated staff who campaigned with such passion and professionalism for Translarna.

Mark Silverman, Trustee

Duchenne research

Research is one of the main elements of the conference and drives all the advances in potential treatments, informing best practice and standards of care. I like to think of aiming to treat Duchenne like an interlinked motorway with dystrophin at its centre. Just recently we have seen the progress in dystrophin restoration replacement strategies, like exon skipping being made available in the US.

The start of these advances was at this conference, building MDEX collaboratively (UK consortium) and funding the early clinical work. The momentum building in gene therapy is also gathering pace, with the realistic hope of clinical trials starting next year. There are also other promising roads in this research motorway; advances in potential cardiac treatments, promoting blood flow to the muscle, driving energy via the mitochondria (the energy powerhouse of the cell), building more healthy muscle, regulating the fine internal balance of calcium and sodium, and stopping the negative feedback loop of inflammation and fibrosis (scarring connective tissue).

All these areas are explored in the conference and much more. The leading international experts from around the world are here over the next two days to answer your questions and get your perspective and input. We know that much more will be achieved as a result of these discussions and we have much more to do to improve the quality of all your lives here today.

Diana Ribeiro, CEO Action Duchenne

Introduction to the Target Roundtables

This year we are holding 'Target Roundtables' on specific topics, covering new strategies, potential treatments and mechanisms in the pipeline.

Muscle and Cell Biology

People with Duchenne have an alteration in the dystrophin gene, known as a mutation. This means they can't produce the protein dystrophin, resulting in a progressive deterioration of muscle strength and function.

Gene Therapy

Gene therapy is an experimental technique aimed to introduce a normal, healthy gene to replace a faulty gene. This could restore the body's ability to produce the correct dystrophin protein. Gene therapy works by using a harmless virus to deliver a functional copy of the gene to the cells. There has been some success delivering small genes, but the dystrophin gene is very big and Prof George Dickson and his team hope to overcome this obstacle by using 2 or 3 viruses; carrying a different part of the gene.

Gene Editing (CRISPR/CAS9)

CRISPR is a genome editing technique used to make precise changes to DNA. There are many different mutations in the dystrophin gene causing Duchenne. Most of these mutations are found in particular regions of the gene, called hot spots. Scientists, using CRISPR technology to cut out large faulty portions of the gene, have found that removal of these portions has resulted in the production of a shorter, but functioning version of the protein. Around 60% of people with Duchenne would potentially benefit.

Stem Cell Therapy

Stem cells are cells which are able to develop into any other type of cells in the body, e.g. muscle cells. Stem cell therapy studies have been conducted in a Duchenne mouse model for effectiveness and safety, but this work is still at an early stage.

Calcium/Sodium Exchange

All our cells require small ions called sodium and calcium ions to be able to function. It is important to have the correct amounts of these ions to prevent muscle cell damage. The sodium-calcium exchange is a small protein found in cells; it removes calcium and allows sodium to enter. Research studies show that in Duchenne there is an overload of both calcium and sodium inside muscle cells. Potential drug treatments are being developed in the hope that muscle function will improve.

Fibrosis

Fibrosis is the process by which damaged tissue is replaced by fat and connective tissue, impeding the ability of the tissue to properly function. Scientists have observed that as fibrosis in muscle tissue increases, the function of the muscle decreases. Researchers are investigating the use of medication, such as anti-fibrotics to reduce fibrosis. It is hoped that this will help those with Duchenne maintain muscle function.

Inflammation

Inflammation is a healthy response known to aid in the cleanup and restoration of damaged muscle. In Duchenne these responses are almost permanently activated and therefore become damaging to the repair process. Steroids are commonly used to treat Duchenne and aim to reduce inflammation to preserve muscle function. However, these drugs often have severe side effects and scientists are working to develop new anti-inflammatory therapies with fewer side effects.

Exon Skipping

A gene is a section of DNA containing instructions for the production of one specific protein. Genes are divided into exons and introns. Exons code for a protein and they are interspersed throughout the DNA alongside introns. When a protein like dystrophin is being produced, the introns are cut out leaving just the exons. These exons are joined together like pieces of a puzzle and when in the correct order, the body can produce the protein. The dystrophin protein has 79 exons and in Duchenne some are deleted. Once the cell realises that one exon is missing, the rest of the exons are not read and the production of dystrophin is terminated.

The aim of exon skipping is to 'skip over' an exon using small 'patches' to mask the exon that we would like to skip. In this way, it is hoped that the rest of the instructions to produce the protein can continue to be read. So far scientists have shown exon skipping to be effective in a Duchenne mouse model and in muscle biopsies from people with Duchenne. One obstacle presented by exon skipping is that each person will require a different exon to be skipped and is not a 'one size fits all' solution.

Other protein targets

Utrophin is a protein, similar to dystrophin and is naturally found in very low levels in the body. Studies suggest that increasing the amount of utrophin could compensate for the lack of dystrophin.

Research is currently taking place to identify small molecules (utrophin up-regulators) that could increase the amount of utrophin in the body.

Rare repurposing in Duchenne

There are many drugs that successfully treat other diseases. Research is currently on-going to investigate if some of these could potentially become treatments for Duchenne. If these already approved drugs can treat Duchenne they could be fast tracked to the clinic for Duchenne patients.

Muscle cellular stress

Muscle cellular stress refers to the way that muscle cells respond when they are exposed to stress, e.g. stress caused by a lack of dystrophin. Cells can either respond by trying to protect themselves or by initiating their own death. The type of response that muscles produce can impact the potential benefit of treatments such as steroids. Research studies to identify how this stress may interfere with other treatments such as gene therapy and how it can be reduced are on-going.

Multimodal pathways in Duchenne

Muscle weakness in Duchenne is often explained by the lack of the protein dystrophin, but dystrophin is not directly responsible. There are multiple pathways which contribute to Duchenne e.g. fibrosis is involved in various pathways which lead to muscle weakness. Fibrosis can rearrange the muscle cells leading to decreased muscle force generation. Fibrosis can also lead to increased distance from blood vessels which supply the muscle cells with oxygen and nutrients. Without sufficient oxygen and nutrients the muscle cells die. Additionally fibrosis perpetuates a continuous inflammatory process, generating scar tissue instead of normal muscle tissue. It is important that these pathways are taken into account to effectively treat Duchenne.

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Friday 11 November

	8.30 - 9.00	9.00 - 9.15	9.15 - 9.55	9.55 - 10.45	10.45 - 11.00	11.00 -11.50	11.50 - 12.40
Plenary Sessions King's (Sandringham) Suite 3rd Floor	Registration (West Wing entrance)	Welcome - King's (Sandringham) Suite 3rd Floor	**Living well and independently** Ros Quinlivan, Jon Hastie, Mark Chapman and Guðjón Reykdal Óskarsson	**Current clinical trial updates** Michela Guglieri	Coffee Break – Monarch (Sovereign) Suite, 1st Floor	**Cardiac (heart) research** John Bourke	**New generation exon skipping updates** Matthew Wood and Aurelie Goyenvalle
DMD Pathfinders Monarch (Viscount) Suite 1st Floor			**Diet research and supplements** Angela Reddy	**Teenage to adult transition (the care aspect)** Ros Quinlivan, Marion Main, Jon Hastie and Mark Chapman		**Assistive services summary and demonstration** Hannah Griffiths, Carl Morris, John Foster, Dean Jose and Geoff Harbach	
Workshop One Rooms 1-6 2nd Floor		Coffee - Monarch (Sovereign) Suite, 1st Floor	**Supporting children and families** David Schonfeld			**Physiotherapy tips** Marion Main	
Target Roundtables Rooms 7-9 2nd Floor			**Inflammation** Michela Guglieri	**Hormones and puberty** Tim Cheetham		**Muscle structure and cell biology** Karl Bettelheim	**Fibrosis** Diana Escolar
Workshop Three Rooms 10-12 2nd Floor			**Overview of clinical trial process** Jordan Butler and Katie Groves	**The ins and outs of taking part in clinical trials** Kate Maurice, Bernie Mooney, Alexandra Johnson and Alex Smith		**A guide to Duchenne genetics** Jo McCauley	**Carrier genetics and support** Sue Kenwrick and Abigail Silverman
Kids' Club Rooms 13-16 2nd Floor	KIDS' CLUB						

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KEY:

1st Floor
2nd Floor
3rd Floor
4th Floor

<table>
<tr><td>12.40 - 14.10</td><td>14.10 - 15.30</td><td>15.30 - 15.40</td><td>15.40 - 16.30</td><td>16.30 - 17.30</td></tr>
<tr><td rowspan="5">World Muscle Society highlights from a researcher perspective and guided research poster session - Monarch (Sovereign) Suite, 1st Floor</td><td>Access to medicines panel session
Nathalie Bere, Daniel O'Connor, Edmund Jessop, Sheela Upadhyaya and Paul Schofield</td><td rowspan="5">Coffee Break – Monarch (Sovereign) Suite, 1st Floor</td><td>Cognitive research and behaviour
Veronica Hinton and Valeria Ricotti</td><td>How to have the best transition to adulthood: lessons from the Takin' Charge project
Janet Hoskin, Celine Barry with young people & families from Takin' Charge and DMD Pathfinders/Steering Committee</td></tr>
<tr><td>Adult health and well-being
Marina Di Marco, Jon Hastie and Mark Chapman</td><td>Sex and relationships
Maddie Blackburn</td><td>Informing children and collecting data: a live clinical trial app demo
Olav Veldhuizen and Cathy Turner</td></tr>
<tr><td>Education Health and Care Plans: getting the right support
Janet Hoskin and Nick Catlin</td><td colspan="2">Company Q&A
Deborah Ascheim - Capricor, Michelle Avery - Summit Plc, Wendy Erler - Wave Biosciences, Justin Fallon - Tivorsan, Sharon Hesterlee - Bamboo Therapeutics, Andrew Napoli - BMS, Florence Porte - Esperare, Carl Morris - Solid Biosciences</td></tr>
<tr><td>Calcuim/sodium exchange
Florence Porte</td><td>Rare repurposing in Duchenne
Steve Winder</td><td>Multimodal pathway in Duchenne
Diana Escolar</td></tr>
<tr><td>DMD registry steering committee (closed sesson)
Angela Stringer</td><td colspan="2">Housing adaptations, your rights and obtaining benefits
Janet Bloor and Mark McGoogan</td></tr>
<tr><td colspan="5">KIDS' CLUB</td></tr>
</table>

Gala dinner at 19:30 in the King's Suite

Saturday 12 November

	8.30 - 9.00	9.00 - 10.00	10.00 - 11.00	11.00 - 11.15	11.15 - 12.15	12.15 - 13.15
Plenary Sessions King's (Sandringham) Suite 3rd Floor	Registration (West Wing entrance)	**Promising new research** Dominic Wells and Stanley Froehner	**Overview of new trials** Thomas Voit	Coffee Break – Monarch (Sovereign) Suite, 1st Floor	**Natural History data: everything you need to know!** Eugenio Mercuri	**Outcome measures in trials** Francesco Muntoni and Marina Di Marco
DMD Pathfinders Monarch (Viscount) Suite 1st Floor		**Physiotherapy tips** Marion Main, Jordan Butler and Marina Di Marco			**Respiratory research** Anita Simonds	**Preventative care (nutrition and ventilation)** Anita Simonds, Angela Reddy, Jon Hastie and Mark Chapman
Workshop One Rooms 1-6 2nd Floor	Coffee - Monarch (Sovereign) Suite, 1st Floor		**What to do in an emergency?** Michela Guglieri		**Standards of care (ages 5-10)** Marion Main and Michela Guglieri	**Standards of care (ages 11-16)** Michela Guglieri, Marion Main and Marina Di Marco
Target Roundtables Rooms 7-9 2nd Floor			**Other protein targets** Kay Davies		**Exon skipping** Annemieke Aartsma-Rus	**Gene therapy** George Dickson
Workshop Three Rooms 10-12 2nd Floor		**Duchenne from the beginning** Annemieke Aartsma-Rus			**Supporting children and families** David Schonfeld	
Kids' Club Rooms 13-16 2nd Floor		KIDS' CLUB				

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KEY:

- 1st Floor
- 2nd Floor
- 3rd Floor
- 4th Floor

13.15 - 14.15	14.15 - 15.15	15.15 - 16.15	16.15 - 17.00
Lunch – Monarch (Sovereign) Suite, 1st Floor	**Genetic replacement technology** Jeff Chamberlain, George Dickson, Xiao Xiao and Ronald Cohn	**Other mutations and protein targets** Kay Davies	**Where are we and what have we learned from recent tirals?** Francesco Muntoni and Thomas Voit
	Respiratory focus group and practical tips Anita Simonds, Jon Hastie and Mark Chapman		**Having carers that are not your parents** Mark Chapman, Jon Hastie, Farhan Mian and Ravi Mehta
	Company Q&A Paolo Bettica - Italfarmaco, Michael Binks - Pfizer Inc, Marc Blaustein - Akashi, Joanne Donovan - Catabasis, Edward Kaye - Sarepta Therapeutics, John Lee - PHASEBio, Marcio Souza - PTC Therapeutics, Jodi Wolff - Santhera Pharmaceuticals		
	Stem cell therapy Jenny Morgan	**Gene editing (CRISPR/Cas9)** Ronald Cohn	**Muscle cellular stress** Keith Foster
	Support for learning and behaviour at school and home Janet Hoskin and Nick Catlin	**Wheelchair access and how to get other services** Dean Jose and Angela Stringer	
KIDS' CLUB			

DMD Pathfinders

As an adult living with Duchenne, I have been involved in raising awareness and funds for research since the 1980s. So much has changed.

When I was diagnosed, my life expectancy was 16, yet I'm now 35. Our management of DMD has improved by leaps and bounds, and there are now more and more adults living with the condition. In the UK, we've joined together to create DMD Pathfinders.

DMD Pathfinders emerged from Action Duchenne's ground-breaking Takin' Charge project, which set out to inspire, encourage and support young people with Duchenne to realise their aspirations. With older adults acting as mentors, it showed us adults how our experiences could be used to make a real difference.

Following our success, Mark Chapman (who is 46 and also living with DMD) and I co-founded DMD Pathfinders as an independent, user-led charity, run by adults with DMD to promote choice and control and quality of life for teenagers and adults also living with the condition.

On care and independent living, we want to support our peers to be able to live fulfilling lives. On research, we want to ensure there are clear pathways for adults to benefit from the new and exciting treatments currently being developed. We certainly have our work cut out for us to ensure the voices of adults are heard!

DMD Pathfinders is delighted to be working with Action Duchenne to deliver a number of conference sessions focused on the needs of adults. We look forward to the many opportunities the conference offers us to work with partners who share our mission.

Jon Hastie, CEO of DMD Pathfinders

Takin' Charge

Action Duchenne's Takin' Charge project successfully ran from 2011 - 2016 and supported 80 young people with DMD between the ages of 14 - 19 years, and their families across the UK. We looked at important issues around growing up such as careers, housing choices, sex and sexuality, developing friendships and being in control of your health. There have been many successes and achievements. However, the main legacy of the Takin' Charge project is the charity DMD Pathfinders, which is the first charity to be set up, run by adults with DMD for adults with DMD. This is a tremendous legacy of the Takin' Charge project.

Takin' Charge culminated in September in a successful Leadership Camp which we ran for young people who have been part of the programme and who put themselves forward as young leaders. The weekend was jointly facilitated and funded by Action Duchenne and DMD Pathfinders. Action Duchenne hopes to continue this partnership with DMD Pathfinders to support teenagers with DMD.

Fundraising

EDM Team:

In May, the Berardelli family took part in Edinburgh Marathon Hairy Haggis Relay as a team of 8! They bounced through the city streets enjoying both the sunshine and the crowd's support as they went. A special moment saw them all finish the event together and take the above group shot with Giorgio, aged 12 and living with Duchenne. The team raised over £4,300 to help continue the search in finding a cure.

It's been another fantastic year for fundraising and raising awareness at Action Duchenne, and we can't thank our community enough for their continuous and amazing support!

Just a few highlights from the last year:

Fundraising in schools

From cake sales to chocolate tombolas, dress down days to sponsored walks, we have been amazed at the ingenuity of the young people who have been fundraising in their schools for us this year.

Duke Street Primary School.

Over 20 schools have participated in events across the country, raising thousands of pounds. Highlights have included Jack Maxwell in Morpeth, and Karsen Ellis in Chorley, who are both living with Duchenne and gave assemblies to their schools about their condition, rousing the pupils into some amazing feats of fundraising. Just these two schools alone raised over £3000.

If you want to fundraise in your local school and want any help getting started just get in touch with our fundraising team who are on hand with all the help and advice you may need.

Dylan Thomas

Tour of Flanders - Martin Savage

This only scratches the surface of what you have done to support Action Duchenne this year - to everyone who has organised balls, dinners, dances and quizzes, sold tickets, put out collection tins, ran, cycled or swam, or set up a direct debit we'd like to say a huge thank you from everyone at Action Duchenne. All the work that we do would not be possible without you.

If you are interested in fundraising for Action Duchenne please talk to any of our staff at the conference, or contact helen@actionduchenne.org

action2016

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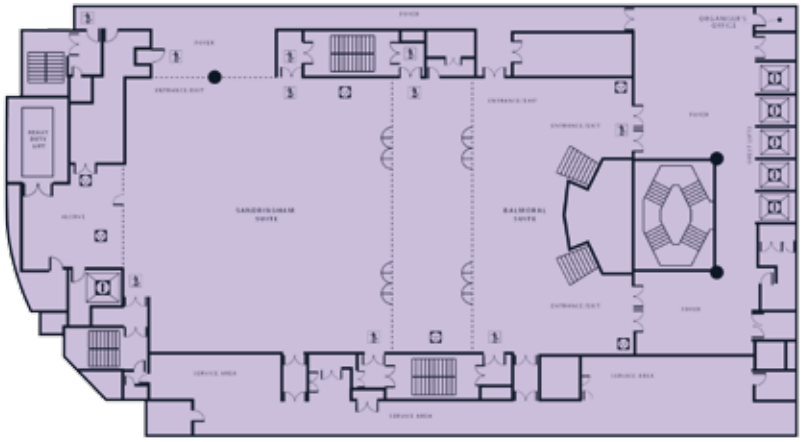
Floor Plans

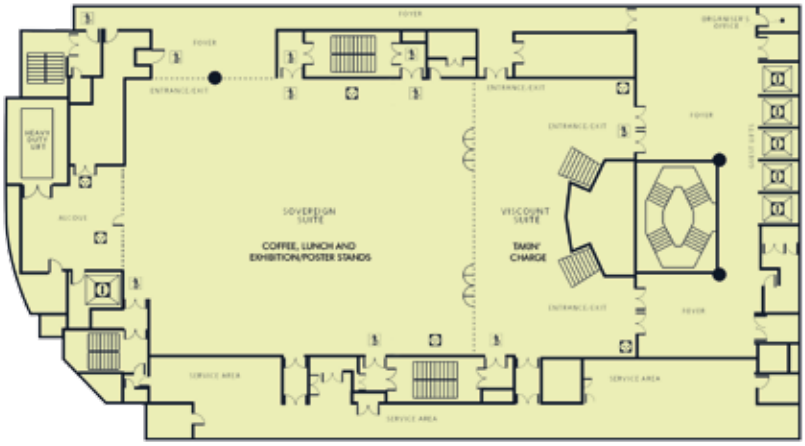
KING'S SUITE

3rd Floor



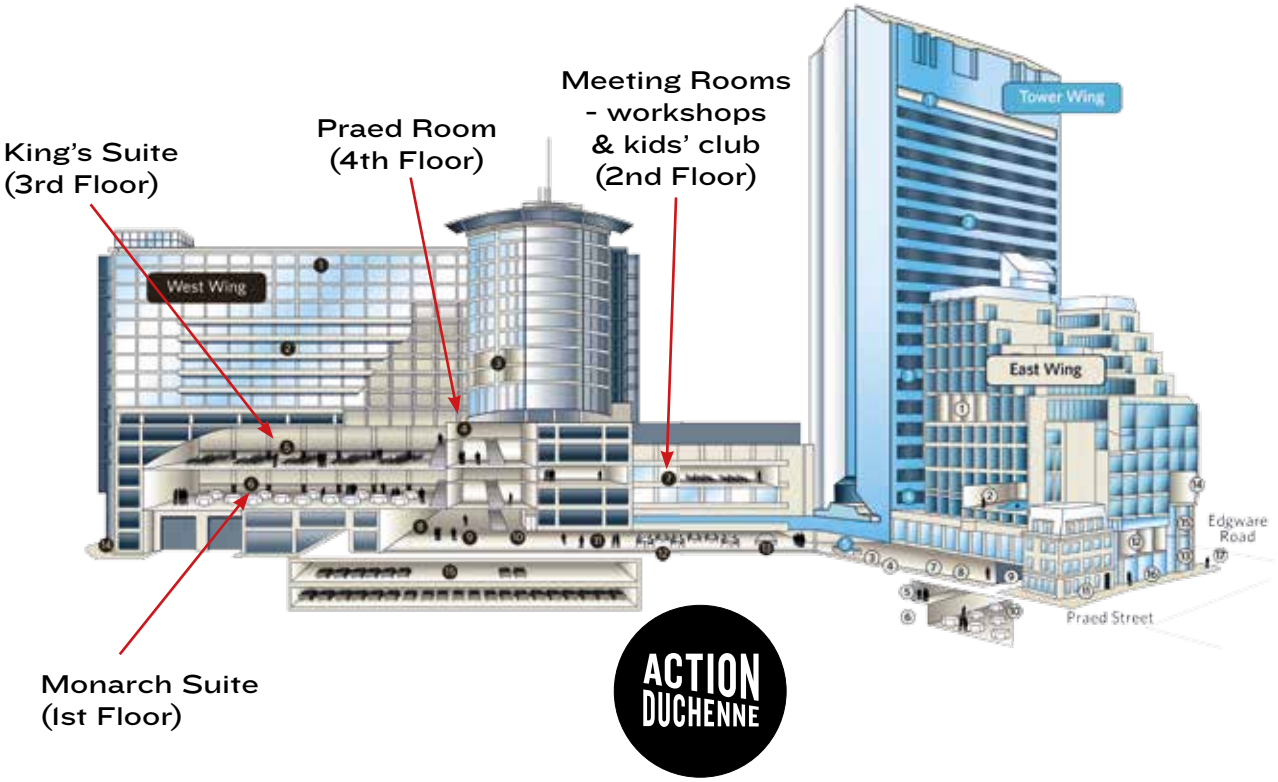
MONARCH SUITE

1st Floor



MEETING ROOMS

2nd Floor



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