

Therapeutic Targets in the CMDs

Thursday, July 9, 2009	
7:30-8am	Breakfast at Whitehead Building
8am-8:20am	Introduction: Anne Rutkowski Introduction and CMD overview: Carsten Bonnemann
Apoptosis 8:20-10:10am	Moderator: Jeffrey Molkentin Paolo Bernardi, Alexei Degterev, Jeffrey Boone Miller
10:10-10:30am	Break
Exercise, Endurance, Metabolism 10:30-12:45pm	Moderator: Vittorio Sartorelli Kevin Campbell, Vihang Nakar, Dan Michele, Ana Ferreiro
12:45-2pm	Lunch
Fibrosis and ECM Signaling I 2-3:50pm	Moderator: Lee Sweeney Se-Jin Lee, Ronni Cohn, Sweta Girgenrath
3:50-4:10	Break
Atrophy, Signaling II 4:10-6pm	Moderator: Denis Guttridge Beth McNally, Orian Shirihai, Beth Barton
6:00-7:15pm	Dinner
Stem and Satellite Cells 7:15-9:05pm	Moderator: Amy Wagers Steve Hauschka, Grace Pavlath, Carsten Bonnemann
Informal meeting 9:15-10:30pm	CMD Care Standards work effort: Ching Wang, Anne Rutkowski
Friday, July 10 th , 2009	
7:30-8am	Breakfast at Whitehead Building
8am-8:15am	Key Note Speaker: Francesco Muntoni Opportunities and Hazards on the Translational Road or How do we avoid too many wrong turns?
Glycosylation, enzyme replacement 8:15-10:30	Moderator: Kevin Campbell Rachelle Crosbie, Paul Martin, Richard Cummings, Lance Wells
10:30-10:50am	Break
Gene therapy 10:50-12:40pm	Moderator: Jeffrey Chamberlain Chunping Quio, Ellen Welch, Markus Ruegg
12:40-1:50pm	Lunch
Inflammatory mediators, Signaling III 1:50-3:40	Moderator: Melissa Spencer Susan Sparks, Marcia Haigis, Dean Burkin
3:40-4:00	Break
Break out sessions 4:00-6:30pm	A. CMD animal models, Preclinical testing standardization. Discussion leaders: Markus Ruegg*, Elizabeth McNally*, James Dowling*, Yiumo Chan* Participants: Dan Michele, Ronni Cohn, Ana Ferreiro, Volker Straub, Alex Mejat, Mon-li Chu, Paolo Bernardi, Steve Moore, Beth Barton, Paolo Bonaldo, Jamie Marshall, Jacintha Rooney

Goals:

1. **Mouse models:**

- a. Compare characterization of available mouse models within each CMD subtype using a consensus battery of phenotypic/histologic/outcome markers
- b. Is there a current mouse model that faithfully replicates disease and can be promoted as a consensus model? If there is not a consensus model, what would the ideal DG or col6 mouse model look like? Could recommendations to KOMP project facilitate development of CMD mouse models?

2. **Zebrafish models:**

- a. Identify list of CMD zebrafish models.
- b. How can zebrafish models be adapted for translational purposes (high throughput drug screens).

3. **Development of Consensus Protocols:**

- a. Fibrosis Evans Blue
- b. Apoptosis
- c. Histologic Assessment
- d. Exercise
- e. Muscle strength
- f. Contracture measurement
- g. Experimental noninvasive techniques to assess drug response

B. CMD Outcome measures/Natural disease progression studies.

Discussion leaders: Richard Finkel*, Eugenio Mercuri*, Kathy Mathews* Enrico Bertini*

Participants: Anne Connolly, Susan Iannaccone, Jiri Vajsar, Susan Sparks, David Eckstein, Ed Trevathan, Valerie Cwik, Susana Quijano-Roy, Ching Wang, Tracy McCausland, Jim Collins, Petra Kaufman, Kevin Flanagan, Thomas Voit, Ed Kaye, Madhuri Hegde, Amy Harper, Sebahattin Cirak, Russ Butterfield

Goals:

- 1. Clinical tool and outcome measures:
 - a. Discuss and design appropriate clinical scales
 - b. Discuss the use of composite scores
 - c. Would it be best to merge composite score and clinical tool?
- 2. Implement prospective natural disease progression study across 4 CMD subtype cohorts (COL6, MDC1A, FKR/ LGMD2I, SEPN1)
 - a. Define the appropriate tools from 1
 - b. Discuss the definition of clinical/functional/age groups of patients across genetic types
 - c. Discuss implementation as a "pilot study"
 - d. Discuss the appropriate use and integration of clinical centers, registries, and funding mechanisms
 - e. Discuss minimum standards of care that will be upheld by participating trial sites to ensure uniformity
 - f. Define best infrastructure plan to collect data: compare UDP, online web resource
- 3. Consider clinical trial design in rare and variable disorders
 - a. Use of the natural history data
 - b. Expansion into clinical trial
 - c. Acceptable primary endpoints

C. CMD translational targets (short term/long term) and role of

	<p>industry. Resource development and screening tools. Discussion leaders: Melissa Spencer* Carsten Bonnemann* Amy Wagers* Jeff Chamberlain*</p> <p>Participants: Kevin Campbell, Sharon Hesterlee, Dean Burkin, Paolo Bernardi, Jeff Molkentin, Jeff Miller, Rachelle Crosbie, Gillian Butler Browne, Gregoire Vuagniaux, Anne Rutkowski, Jon Tinsley, Bradley Hodges, Paul Martin, Francesco Muntoni, Glen Nuckolls, Vihang Nakar, Vittorio Sartorelli, Marcia Haigis, Orian Shirihai, Steve Hauscka, Ellen Welch, Dennis Guttridge, Se-Jin Lee, Lee Sweeney, Rich Cloud, Kurt Fischbeck, Chris Austin, John Porter, Richard Cummings, Lance Wells, Pat May, Sandrine Arbogast, Alessia Angelin, Ajay Kumar, Grace Pavlath, Johan Holmberg, Carol Nelson</p> <p>Goals:</p> <ol style="list-style-type: none"> 1. Short term targets (moderator- Melissa Spencer) <ol style="list-style-type: none"> a. Identify promising targets (with synergistic developmental potential) b. Define necessary steps forward for each target to proof its validity and to evaluate it in preclinical testing 2. Long term targets (moderator- Jeff Chamberlain) <ol style="list-style-type: none"> a. Decide on promising targets b. What would constitute proof of principle for such a target? c. What are the opportunities for synergies to accelerate development? 3. High throughput screening (moderator- Amy Wagers) <ol style="list-style-type: none"> a. For which target would HTS be appropriate? b. How can assays be developed and validated?
6:30-8pm	Dinner
Plenum post break-out 8:00-10:30pm	<p>Break out session Action Plans presented to plenum by discussion leaders:</p> <p>8:00-8:20 Presentation Breakout Animal Model group</p> <p>8:20-8:35 Plenum discussion on animal models</p> <p>8:35-8:55 Presentation Breakout Natural Disease Progression group</p> <p>8:55-9:10 Plenum discussion on Natural Disease Progression/outcome markers</p> <p>9:10-9:25 Presentation Short Term Therapeutic Targets and Suitability for HTS</p> <p>9:25-9:40 Presentation Long Term Therapeutic Targets and Suitability for HTS</p> <p>9:40-10:15 Plenum discussion on short and long term target investments</p>
Saturday, July 11, 2009	
7:30am-8:00am	Breakfast
8:00-8:15am	Introduction: Cure CMD
Clinical trial design in rare disorders 8:15-10:10am	<p>Moderator: Kurt Fischbeck</p> <p>Petra Kaufmann, Francesco Muntoni, Richard Finkel</p>
10:10-10:30am	Break
CMD “toolkit” panel 10:30-12:30 10 minute discussion followed by 30 minute panel	<p>Moderator: Glen Nuckolls*, John Porter*</p> <p>Panel: Steve Moore* (<i>U of Iowa Biorepository</i>), Ed Trevathan* (<i>CDC- MD STAR net, epidemiological studies in rare disease</i>), Volker Straub* (<i>TREAT-NMD Drug Throughput committee, TACT</i>), Vanessa Rangel Miller* (<i>CMD International Patient Registry</i>), Ellen Welch* (<i>Pharmaceutical perspective</i>), Chris Austin* (<i>high throughput screening assays</i>), Madhuri Hegde* (<i>CMD High Throughput</i>)</p>

discussion	<i>Genetic Test)</i>
12:30-1:15	Bag Lunch
Pharmaceutical Industry Perspective 1:15-3:30pm	Moderator: Ed Kaye* (Genzyme) Brad Hodges* (Prothelia), Ronald Farkas*(FDA), Jon Tinsley* (Summit PLC), Jane Larkindale (MDA VP)*
Conference Summary 3:30-3:45 pm	Carsten Bonnemann closing remarks

Saturday, July 11, 2009 Afternoon 4-6pm	Cure CMD SMAB: Carsten Bonnemann, Volker Straub, Francesco Muntoni, Markus Ruegg, Alexandre Mejat, Ed Kaye, Anne Rutkowski
Agenda	Ratify SMAB policies
(Auditorium)	Translational Roadmap
	Drug Pipeline, RFA

Saturday, July 11, 2009 Dinner, CMD clinical consortium 7-10pm Bus at 7pm Woodruff Residential center	Informal meeting: CMD Consortium: Launch Outcome measures and Natural Disease progression Carsten Bonnemann, Kathy Mathews, Volker Straub, Enrico Bertini, Eugenio Mercuri, Ana Ferreiro, Susan Iannaccone, Anne Connolly, Jim Dowling, Jim Collins, Kevin Flanigan, Ching Wang, Valerie Cwik, Rich Finkel, Markus Ruegg, Petra Kaufman, Glen Nuckolls, Anne Rutkowski, Pat May, Rich Cloud, Ronald Farkas, Tracy McCausland, Amy Harper, Jon Tinsley, Alessia Angelin, Sue Brown
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