

Tentative workshop schedule (confirmed participants are marked by *)

| Thursday, July 9, 2009 | |
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| 7:30-8am | Breakfast at Whitehead Building |
| 8am-8:20am | Introduction: Anne Rutkowski* Introduction and CMD overview: Carsten Bonnemann* |
| Apoptosis 8:20-10:20am | Moderator: Jeffrey Molkentin* Paolo Bernardi*, Alexei Degterev*, Jeffrey Boone Miller* |
| 10:20-10:35am | Break |
| Fibrosis, ECM signaling 10:35-1pm | Moderator: Lee Sweeney* Se-Jin Lee*, Ronni Cohn*, Beth Barton*, Sweta Girgenrath* |
| 1-2pm | Lunch |
| Atrophy 2:00-3:35pm | Moderator: Denis Guttridge* Beth McNally*, Orian Shirihai* |
| Exercise and Endurance 3:35-6pm | Moderator: Vittorio Sartorelli* Kevin Campbell*, Vihang Nakar*, Dan Michele*, Ana Ferreiro* |
| 6:00-7:30pm | Dinner |
| Stem and Satellite Cells 7:30-9:15pm | Moderator: Amy Wagers* Steve Hauschka*, Grace Pavlath* |
| Informal meeting 9:15-10:30pm | CMD Care Standards work effort: Ching Wang* Anne Rutkowski* |
| Friday, July 10, 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 8:15-10:40 | Moderator: Kevin Campbell* Rachelle Crosbie*, Paul Martin*, Richard Cummings*, Lance Wells* |
| 10:40-10:55am | Break |
| Gene therapy 10:55-12:55pm | Moderator: Jeffrey Chamberlain* Carsten Bonnemann*, Ellen Welch*, Markus Ruegg* |
| 1:00-2:00pm | Lunch |
| Inflammatory mediators, other signaling targets 2:00-3:40 | Moderator: Melissa Spencer* Susan Sparks*, Marcia Haigis*, Dean Burkin* |
| 3:40-4:00 | Break |
| Break out sessions 4:00-6:30pm | <p>A. CMD animal models, Preclinical testing standardization. Discussion leaders: Markus Ruegg*, Elizabeth McNally*, James Dowling*, Yiumo Chan*</p> <p>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</p> <p>Goals:</p> <ol style="list-style-type: none"> 1. Mouse models: <ol style="list-style-type: none"> 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: <ol style="list-style-type: none"> 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: <ol style="list-style-type: none"> 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 Flanigan, 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 industry.

Resource development and screening tools. Discussion leaders: Melissa Spencer* Carsten Bonnemann* Amy Wagers* Jeff Chamberlain*

Participants: Kevin Campbell, Sharon Hesterlee, Dean Burkin, Paolo Bernardi, Jeff Molkentin, Jeff Miller, Rachele 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 Shirihi, 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

Goals:

1. Short term targets (moderator- Melissa Spencer)
 - 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)
 - 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)
 - a. For which target would HTS be appropriate?
 - b. How can assays be developed and validated?

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| Plenum post break-out 8:00-10:30pm | Break out session Action Plans presented to plenum by discussion leaders: 8:00-8:20 Presentation Breakout Animal Model group 8:20-8:40 Plenum discussion on animal models 8:40-9:00 Presentation Breakout Natural Disease Progression group 9:00-9:20 Plenum discussion on Natural Disease Progression/outcome markers 9:20-9:40 Presentation Short Term Therapeutic Targets 9:40-10:00 Presentation Long Term Therapeutic Targets 10:00-10:30 Plenum discussion on short and long term target investments |
| Saturday, July 11, 2009 | |
| 7:30am-8:00am | Breakfast |
| 8:00-8:15am | Introduction: Cure CMD |
| Clinical trial design in rare disorders 8:15-10:10:15 | Moderator: Kurt Fischbeck* Petra Kaufmann*, Francesco Muntoni*, Richard Finkel* |
| 10:15-10:30am | Break |
| CMD "toolkit" panel 10:30-12:30 10 minute discussion followed by 30 minute panel discussion | Moderator: Glen Nuckolls*, John Porter* 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>), Valerie Cwik* (<i>MDA perspective/resources</i>), Chris Austin* (<i>high throughput screening assays</i>), Madhuri Hegde* (<i>CMD High Throughput Genetic Test</i>) |
| 12:30-1:15 | Bag Lunch |
| Pharmaceutical Industry Perspective 1:15-3:20pm | Moderator: Ed Kaye* (Genzyme) Brad Hodges* (Prothelia), Ronald Farkas*(FDA), Jon Tinsley* (Summit PLC), Jane Larkindale (MDA VP)* |
| Conference Summary 3:20-3:30 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 |
| | Translational Roadmap |
| | Drug Pipeline, RFA |
| Saturday, July 11, 2009 Dinner, CMD clinical consortium 7-10pm | 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 |