Meeting Description

SASS2023 is the inaugural of an annual sarcoma conference: "Strategic Advances in Sarcoma Science". This conference meets at the NIH campus (Bethesda, MD) on Sept 14-15, 2023, and is co-sponsored by the Center for Cancer Research, NCI. The SASS2023 organizing group is the SARC Discovery/Translation committee (www.tinyurl.com/SARC-DTC).

SASS2023 has eight main sessions focused on basic science and four breakouts focused on translational/clinical challenges. This collaborative conference aims for a fun and interactive workshop-like experience but at somewhat larger scale (120 participants). Differentiating features of the conference include emphases on continuity and deliverables. The SARC DTC is raising funds to subsidize pilot projects in the breakout groups and to defray travel/lodging expenses for early career participants. The SASS registration fee is \$100 (to defray meal, AV, and other costs) and is waived for those attending only a Breakout session.

SASS MAIN SESSIONS

- 1. Models: Novel Approaches and Applications
- 2. Omics: New Twists, New Therapeutic Challenges
- 3. Sarcoma Immune and Non-Immune Interactions
- 4. Sarcoma Metabolism
- 5. Dissecting Sarcoma Progenitors and Evolution
- 6. Epigenetic Mechanisms in Sarcoma
- 7. BAF Dysregulation in Sarcoma
- 8. Reapproaching Sarcoma Cytotoxicity

BREAKOUT GROUPS

- 1. GIST
- 2. Sarcoma Research Consortia
- 3. Immune Biology and Immunotherapies
- 4. Advances in Sarcoma Therapies: Delivery, Strategies, Targets

September 14

9:00 Conference Introduction/Overview:

- main session presentations are <u>10 minutes</u> and emphasize mechanistic science: define opportunities for interaction/collaboration. Less emphasis on recent data (refer to publications instead of showing lots of data). Think-tank approach. Highlight key challenges. Science, but highlight opportunities to enhance correlative science and foster creative/nimble trials.

- conference aims: interactivity, deliverables, continuity between annual meetings

9:10-10:10 Session #1: Models: novel approaches + applications

Moderator: D. Wade Clapp (Indiana U) – intro: limitations and opportunities 1a. Roland Imle (Heidelberg) – new models for pediatric sarcoma 1b. Rebecca Dodd (U Iowa) – advances with GEMMs in NF1 sarcomas 1c. Jason Yustein (Emory) – advances with GEMMs in bone sarcomas Discussion: ~25 min (for all main sessions, might be useful for moderator to restate/show key questions)

10:10–11:20 Session #2: Omics – new twists, new therapeutic challenges

Moderator: Jonathan Fletcher (Harvard) – *Introduction*: 5 min 2a. Lily Guenther (St. Jude's) – functional genomic insights in bone sarcomas 2b. Christine Pratilas (Johns Hopkins) – escape mechanisms for MEK targeting 2c. Jack Shern (NCI) – cell-free DNA: from clinical tool to mechanism 2d. Sebastian Bauer (Essen) – apple mutations in GIST Discussion: ~25 min

11:10-11:30 BREAK

11:30-12:50 BREAKOUT GROUPS

13:00-13:45 LUNCH

13:45-15:00 Session #3: Sarcoma immune and non-immune interactions

Co-moderator: Troy McEachron (NCI) non-immune microenvironment 3a. Troy McEachron (NCI) 3b. Rosandra Kaplan (NCI) – pre-metastatic niche, stromal microenvironment Discussion: ~15 min Co-moderator: Seth Pollack (Northwestern) – altering the sarcoma immune microenvironment for therapy 3c. Lauren Banks (MSKCC) – sarcoma immune microenvironment 3d. Daniel Regan (Colorado State): fibroblasts/macrophages in canine osteosarcoma microenvironment Discussion: ~15 min

15:00-15:15 BREAK

15:15-16:30 Session #4: Sarcoma metabolism

Moderator: Joanna Przybyl (McGill) – *Introduction*: 5 min 4a. Christine Heske (NCI) – challenges, opportunities 4b. Kathryn Lemberg (Johns Hopkins) – targeting glutamine metabolism 4c. Brian van Tine (Wash U) – preventing arginine starvation from preventing apoptosis 4d. Ben Alman (Duke) – IDH mutation metabolic consequences Discussion: ~25 min

16:30–17:45 Session #5: Dissecting sarcoma progenitors and evolution

Moderators: Brigitte Widemann & Jack Shern (NCI)

5a. Matt van de Rijn (Stanford) – field effects in mesenchymal neoplasia

5b. Ariadna Brito (Toulouse) - cell fusion in sarcomagenesis

5c. Richard Lu (Cincinnati Children's) – MPNST progenitors and evolution

5d. David Langenau (Harvard) – cell heterogeneity and therapy responses in rhabdomyosarcoma Discussion: ~25 min

18:00–20:30 Poster Session & Dinner

19:30–20:30 Proffered Posters (Moderators/Discussants: Elizabeth Demicco, Lee Helman) Single cell studies – Tiffany Eng, Anand Patel, Corey Weistuch: 5 min each + 15 min group discussion. Models – Janai Carr-Ascher, Jason Chan, Roland Imle: 5 min each + 15 min group discussion.

September 15

7:30-8:00 Light Breakfast

8:00-9:40 Breakout Group summaries and discussion

(10 min summaries + 15 min discussion per breakout)

9:40-10:00 Break

10:00-11:00 Session #6: Epigenetic mechanisms in sarcoma

Moderator: Benjamin Nacev (U Pittsburgh) – *Introduction*: 5 min 6a. Benjamin Nacev (U Pittsburgh) – alterations in epigenetic regulators are common in sarcomas - how can we leverage this to help patients? 6b. Berkley Gryder (CWRU) – small molecules that exploit epigenetic vulnerabilities in AYA sarcomas

6c. Yong Yean Kim (NCI) – epigenetics of fusion oncogene driven sarcomas Discussion: ~25 min

11:00–12:00 Session #7: BAF dysregulation in sarcoma

Moderator: Kevin Jones (Huntsman) – *Introduction*: 5 min 7a. Kevin Jones (Huntsman) – BAF family complexes componentry in synovial sarcoma 7b. Siddhant Jain (Harvard) – Structure and Function of Mammalian SWI/SNF Chromatin Remodeling Complexes in Synovial Sarcoma 7c. Alex Kentsis (MSKCC) – towards rational epigenetic combination therapy of rhabdoid tumors Discussion: ~25 min

12:00-12:45 LUNCH

12:45-1:45 Session #8: Reapproaching sarcoma cytotoxicity

Moderator: Rebecca Gladdy (U Toronto) – *Introduction*: 5 min 8a. Ping Chi (MSKCC) – enhancing cytotoxicity by viral mimicry 8b. Philipp Novotny (Heidelberg) – enhancing cytotoxicity by RTK inhibition 8c. Adrian Marino-Enriquez (U College Dublin) – enhancing cytotoxicity while reigning in toxicity Discussion: ~25 min

1:45-2:15 Conclusions and next steps

- conference size, structure, themes, and duration. What should be changed?
- deliverables
- feedback is crucial (drop off evaluation forms before leaving)

Breakout Groups

The SASS breakout groups have a <u>therapeutics/clinical</u> focus with well-defined <u>deliverables</u>. Additional meetings are held before/after SASS to accomplish the deliverables.

SASS 2023 Breakout Groups:

1. Gastrointestinal Stromal Tumor (GIST): Sebastian Bauer (Essen), Ping Chi (MSKCC), Andy Wagner (DFCI). Early-career co-leads: Candace Haddox (DFCI), Thomas Mühlenberg (Essen), Joanna Przybyl (McGill)

This multidisciplinary group defines emerging therapeutic challenges in patients whose GISTs are progressing on approved TKI drugs.

<u>Deliverables:</u> 1) GIST state-of-the-science review; 2) co-organize, with FORTRESS, an international stand-alone multidisciplinary GIST basic and clinical research conference: October 17-18, 2024 (Essen, Germany).

2. Sarcoma Research Consortia: Katie Janeway (DFCI/Boston Children's), Sam Singer (MSKCC), Jonathan Fletcher (SARC). Early-career co-leads: Ariadna Brito Accurso (Toulouse INSERM), Josephine Dermawan (Cleveland Clinic), Roland Imle (Heidelberg)

Brings together representatives of multi-institutional sarcoma research programs to define opportunities for inter-program collaboration. The programs include three NCI SPOREs (HyperRas SPORE, MSKCC SPORE, and LMS SPORE), Advocacy group representatives, The Osteosarcoma Institute, Count Me In, LMS Roundtable, DF PDGFRA GIST Program, Harvard David Liposarcoma Program, NCI Clinical Proteomic Tumor Analysis Consortium (CPTAC), SARC, Sunshine Project, and TARPSWG. <u>Deliverables:</u> 1) on-line compilation of sarcoma research consortia, foundations, advocacy groups, and funding sources; 2) an organization "SASSy" that connects early-career sarcoma investigators: collaborations and conferences.

3. Immune biology and Immunotherapies: Ron DeMatteo (Penn), Seth Pollack (Northwestern), Bree Wilky (U Colorado). Early-career co-leads: David Milewski (NCI), Jacqueline Oliva Ramírez (MDACC).

Defines novel strategies to be explored in development of immunotherapies of sarcoma subtypes. This includes development of combination approaches for subtypes that have been heretofore refractory to immunotherapy as well as target identification and sarcoma-specific technology development for cellular therapies. Also includes creation of immunocompetent GEMMs to facilitate immunotherapy development and enable studies of the sarcoma immune microenvironment.

Deliverable: pilot concepts will be further developed during SASS2024 (September 2024).

4. Advances in Sarcoma Therapies – Delivery, Strategies, Targets: Suzanne George (DFCI), Margaret von Mehren (FCCC), Brigitte Widemann (NCI). Early-career co-leads: Priscila Barreto Coehlo (Sylvester), Lily Guenther (St. Jude), Jan Philipp Novotny (Heidelberg).

Brings together sarcoma researchers and members of CTEP and the FDA to examine opportunities and define priorities for maximizing sarcoma therapeutic response through newer drug approaches, selective drug delivery, and/or drug targets not previously tested in sarcoma. This breakout also enables lab scientists to obtain guidance from seasoned sarcoma clinical trialists. Opportunities to maximize response to newer strategies will be defined and expanded upon in subsequent SASS conferences: protein degraders, γ -secretase inhibitors, HIPPO pathway inhibitors as examples.

Deliverable: state-of-the-science review on achieving more effective trial designs for sarcoma.

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The SASS2023 organizers (SARC Discovery/Translation Committee) express their deep appreciation to our co-sponsors for their enthusiasm and kindness – enabling this inaugural SASS conference and the post-SASS pilot projects and publications!

