CoC Cancer Liaison Physicians Meeting

Quyen Chu, MD, FACS
Chair
Committee on Cancer Liaison

Maria Castaldi, MD, FACS
Vice-Chair
Committee on Cancer Liaison
Meeting Logistics

• All participants, except presenters, are muted during the webinar.

• Questions – including technical issues you may be experiencing – should be submitted through the question pane.

• Questions will be answered as time permits; we will respond to any questions we aren’t able to address during the meeting.

• We will post the recording of this meeting on the CLP page of our website.
CoC 100th Anniversary

100 Years of Advancing Cancer Care

Commission on Cancer | 1922–2022
Welcome New CoC State Chairs

Jeanne Capasse
MD, FACS
Connecticut

Jeffrey Farma
MD, FACS
Metro Philadelphia

Sara Fogarty
DO, FACS
Maryland

Katie Fritz
MD, FACS
Idaho

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Welcome New CoC State Chairs

Ajay Jain
MD, FACS
Oklahoma

Shannon Orr III
MD, FACS
Mississippi

Alberto Pena
MD, FACS
South Texas

Sushanth Reddy
MD, FACS
Alabama
Welcome New CoC State Chairs

Rocco Ricciardi
MD, FACS
Massachusetts

Richard Royal
MD, FACS
Maine

Vassiliki Tsikitis
MD, FACS
Oregon

Jason Wilson
MD, MBA, FACS
Florida
CoC Cancer Liaison Physicians
Outstanding Performance Awards
CLP Outstanding Performance Awards

Samuel Carvajal, MD, FACS
Adventist Health
Glendale, CA

Babak Eghbalieh, MD, FACS
Providence Holy Cross Medical Center
Mission Hills, CA
CLP Outstanding Performance Awards

David Mullins, MD, MBA, CPE, FACS
Princeton Community Hospital
Princeton, WV

Sangeetha Prabhakaran, MBBS, FACS
UNM Comprehensive Cancer Center
Albuquerque, NM
CLP Outstanding Performance Awards

Tracy Rauch, MD
Our Lady of the Lake Regional Medical Center
Baton Rouge, LA

Anthony Strawn, MD, FACS
Fort Belvoir Community Hospital
Fort Belvoir, VA
CLP Outstanding Performance Awards

Raquel Wagman, MD
The Cancer Center at Saint Barnabas Medical Center
Livingston, NJ

Michael Whalen, MD
George Washington University Hospital
Washington, DC
CLP Outstanding Performance Awards

Jason Wilson, MD, MBA, FACS
Morton Plant Mease Health Care
Palm Harbor, FL

Anthony Yang, MD, MS, FACS
Northwestern Memorial Hospital
Chicago, IL
CoC Update

- **New NCDB resources**
  - Comprehensive NCDB Tools Brochure
  - Video Education Series
- **New Patient Brochure**
  - Educate your patients on the benefits of seeking treatment at an accredited center
  - Can be customized for your program
- **Coming Soon:**
  - New CLP Best Practices Guide
  - CLP Survey
- **CoC Plenary Session**
  - Tomorrow (October 20), 2:15 – 4:15 pm CT
  - [coc@facs.org](mailto:coc@facs.org)
CoC Update

Quality Webinars
Daniel Boffa, MD, FACS,
Chair, CoC Quality Integration Committee
Accreditation Update

- Synoptic Operative Standard Implementation
- Review of Changes/Updates to CoC 2020 Standards
- Q Port Update
CoC Operative Standards Resources Update

CSSP Education Committee

Chair, Mediget Teshome MD MPH FACS
Vice-Chair, Timothy Vreeland MD FACS

CoC Cancer Liaison Physicians Meeting
10.19.2021
Recently Released Resources

- Fillable PDF forms for Standards 5.3, 5.4, 5.5, and 5.6

**Accessed through the Standards Resource Library via Datalinks**
# Recently Released Resources

## Commission on Cancer Operative Standards 2020

### Synoptic Operative Reports: CoC Standards 5.3–5.6

<table>
<thead>
<tr>
<th>Definition</th>
<th>Benefits</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized sets of data elements organized as a structured checklist or template</td>
<td>Allow information to be easily collected, stored, and retrieved, resulting in:</td>
<td>2022&lt;br&gt;Programs document final plan for implementation</td>
</tr>
<tr>
<td>Each data element’s value is filled in using a pre-specified format</td>
<td>Accuracy&lt;br&gt;Efficiency of entry&lt;br&gt;Efficiency of data abstraction</td>
<td>2023&lt;br&gt;Operative reports must meet technical &amp; synoptic formatting requirements</td>
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<tr>
<td></td>
<td>Variability&lt;br&gt;Costs</td>
<td>2024&lt;br&gt;Site visits assess 2023 reports for 70% compliance</td>
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<tr>
<td></td>
<td>... thereby increasing the quality of cancer care</td>
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Download from the [Operative Standards Toolkit](https://facs.org/cssp)!
Recently Released Resources

• Brief videos on the CoC Operative Standards:
  • CoC Standard 5.7: Requirements & Best Practices
  • Synoptic vs. Narrative Operative Reports
  • Synoptic Operative Reporting Roadmap

• Behind the Knife podcast – Ep. 392: ACS Cancer Surgery Standards Program

• 2022 Site Visit Preparation for Standards 5.7 & 5.8 – Webinar held on 8/30/2021 (recording, slides, and summary document available online)

• Guidelines documents for registrars on Standards 5.3-5.6 coming soon!

Bookmark the Operative Standards Toolkit for the latest resources!
Synoptic Operative Reporting
Now and in the Future

1. First phase of synoptic operative report (SOR) development and implementation via local or third-party vendor solutions

2. Comprehensive set of SOR content developed covering all disease sites represented in surgical oncology

3. Universal implementation of structured SORs

4. EMR-integrated SORs allowing for data sharing across groups, automated data abstraction, and improved quality

facs.org/cssp
Timeline for Standards 5.3-5.6

- **Plan for implementation, educate/train surgeons & registrars**
- **Document final plan for implementation and conduct audits**
- **Begin compliance with Standards 5.3-5.6**
- **Site Reviews**
- **Site Visits review documentation of final plans for compliance**
- **Site Visits review 2023 operative reports for 70% compliance**
- **Site Visits review 2023 & 2024 operative reports for 80% compliance**

**Steps to Achieve Compliance**
Upcoming Events

CoC Plenary

Wednesday, October 20th @ 2:15 - 4:15p CT

Operative Standards Implementation

Moderator: Matthew H.G. Katz MD FACS
Panelists: Requirements - James Harris MD FACS
Surgeon Awareness Survey - Tim Vreeland MD FACS
Educational Resources - Mediget Teshome MD FACS
Implementation Timelines/Strategies - Tina Hieken MD FACS
Upcoming Events

CSSP Webinar on Breast Standards 5.3 & 5.4

Wednesday, November 17th @ 3:00 – 4:00p CT

A multidisciplinary panel will discuss the requirements and purpose of CoC Standards 5.3 and 5.4, best practices for achieving compliance, and the role of evidence-based standards in improving outcomes for patients with cancer.

Registration is required: tinyurl.com/CSSPbreastwebinar
Questions?

cssp@facs.org

Quick Links:
Operative Standards Toolkit
CoC 2020 Operative Standards
CAnswer Forum
Review of Changes/Updates to CoC

2020 Standards for 2022

James Harris, MD, FACS
Erin DeKoster, JD, MS
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<th>Accredited-Corrective Action Required (Renewal Programs Only)</th>
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<td>All standards compliant</td>
<td>Awarded when a renewal program receives a noncompliant rating on at least one standard but less than 20% of standards rated during the site visit process.</td>
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<tr>
<td></td>
<td>• Program appears on Find an Accredited Program website</td>
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<tr>
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<td>• Certificate of accreditation awarded</td>
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<td></td>
<td>• Included on Find an Accredited Program website</td>
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<td>• 1 year to resolve noncompliant standards</td>
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<td>• Program receives a certificate once all standards have been resolved and “Accredited” status has been achieved</td>
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<td>Awarded when a new program, including new INCPs or NCINs consisting of currently accredited programs, receives a noncompliant rating on one or two standards during the site visit process.</td>
<td>Awarded when:</td>
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<tr>
<td>• Not included on Find an Accredited Program website</td>
<td>• Renewal program receives a noncompliant rating on more than 20% of standards rated during the site visit process</td>
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<tr>
<td>• 1 year to resolve noncompliant standards</td>
<td>• Initial applicant receives three or more noncompliant standards</td>
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<td></td>
<td>• Program does not resolve non-compliant standards within established timeframe.</td>
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<tr>
<td>Awarded when:</td>
<td>• No access to the Quality Portal or NCDB tools</td>
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<tr>
<td> Renewal program receives a noncompliant rating on more than 20% of standards rated during the site visit process</td>
<td>• Program may re-apply as an initial applicant program after one calendar year of compliance to all applicable standards</td>
</tr>
<tr>
<td> Initial applicant receives three or more noncompliant standards</td>
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Standard 6.5: Follow Up of Patients

Long term follow up now a rolling 15-year requirement (80% requirement)
  • NCDB will not collect follow up information for cases older than 15 years from the most current year of completed cases

Short term follow up continues to be 5 years from most current year of completed cases (90% requirement)

Example for 2022
  • Long term: cases diagnosed 2006 to 2020 (80% requirement)
  • Short term: cases diagnosed 2016 to 2020 (90% requirement)

Example for 2023
  • Long term: cases diagnosed 2007 to 2021 (80% requirement)
  • Short term: cases diagnosed 2017 to 2021 (90% requirement)
Guidelines for forming a network have been updated, including minimum requirements and steps for forming a network.

2020 CoC Standards reviewed and revised as they apply to INCP/NCIN to address integration and distribution of services across the network and its facilities.

New INCP/NCIN Standards Implementation:

- Current networks must implement by January 1, 2023 (first reviewed at 2024 site visits)
- New networks must implement by January 1, 2022 (first reviewed at 2023 site visits)
Starting in 2022, programs must document their plan in the cancer committee minutes for how they will implement the following standards:

- 5.3: Sentinel Node Biopsy for Breast Cancer,
- 5.4: Axillary Lymph Node Dissection for Breast Cancer,
- 5.5: Wide Local Excision for Primary Cutaneous Melanoma, and
- 5.6: Colon Resection

Plans will be first reviewed at 2023 site visits.
Where to find more information

Full text of changes to accreditation outcomes, Standard 6.5 and the network standards available for download: facs.org/2020cocstandards

Changes will be incorporated into Optimal Resources for Cancer Care (2020 Standards) in November 2021.

Comprehensive list of implementation timelines for all standards: facs.org/cocstandardsupdates
CoC QPort Update

Welcome to QPort
The American College of Surgeons Quality Portal

Vicki Chiappetta, RHIA, CTR
Senior Accreditation Specialist
Cancer Programs
Logging On

https://qualityportal.facs.org/qport

- Use your existing Username and Password
- Login Credentials are the same for all Quality Programs and American College of Surgeons Membership
- The Forgot Password Link should be used to reset or retrieve your password
QPort Menu

Primary Contact adds/edits/removes contacts. This is for read-only access to RCRS.

Allows for sharing of documents between site and CoC Staff. Not part of PRQ.

Primary Contact adds/edits/removes contacts. Be sure your information is up to date. Gives access to Qport.

PRQ is available the year program is due for site visit.

Previous PRQs & Accreditation Reports

Page for all Qport, standards, and site visit resources
Accreditation Fees
Forms
Standards Updates
Site Visit Resources
Templates & Worksheets
Site Reviewer Profiles
Instructional Resources
Appeals, Corrective Action
NCDB links (CoC only)
Standards Resource Library (CoC only)
Site Visit Experience Survey
Marketing Resources

Site Visit Resources
- Blank pdf of CoC PRQ
- Required Documents for the PRQ
- Checklist for 2020 Standards
- Site Visit Agenda and Instructions
- Reference Date Change information
- Site Reviewer Profiles
- CoC Appeals Instructions
- CoC Appeals Form
- Corrective Action Instructions
- Corrective Action Documentation
- Accountability and Quality Improvement Measures for 2022 Site Reviews
- Accreditation Outcomes (Awards)
- Survey Extension or Cancellation Policy
- COVID-19 Accreditation Tracker (blank)
- COVID-19 Accreditation Tracker (example)
- Site Visit Experience Survey (To be completed within 14 days of site visit)
Thank you

coc@facs.org
CoC Paper Competition Winners: Clinical Research

1st Place:  
Sarah Kaslow, MD  
NYU Langone  
“Patient- and hospital-level determinants of guideline-adherent care have a significant impact on overall survival for patients with gastric cancer. An analysis of the National Cancer Database”

2nd Place:  
Michael Poulson, MD  
Boston University/Boston Medical Center  
“Segregation, Colorectal Cancer, and Socioeconomic Mediators: A Structural Equation Modeling Approach”

3rd Place:  
Daniela Cocco, MD  
Cleveland Clinic Foundation  
“Can axillary lymph node dissection be omitted in patients with limited clinically node positive breast cancer?”
CoC Paper Competition Winners: Basic Science

1st Place:

David Hanna, MD
Vanderbilt University Medical Center
“RSL3 Induces Ferroptosis via GPX4 Inhibition in Papillary Thyroid Cancer”

Garrett Steers, MD
University of Iowa
“Epigenetic Changes in Pancreatic Cancer with Pharmacologic Ascorbate.”
RSL3 Induces Ferroptosis via GPX4 Inhibition in Papillary Thyroid Cancer

David N. Hanna, Konjeti R. Sekhar, Sriram Cyr, Sudhakiranmayi Kuravi, Ramesh Balusu, W. Kimryn Rathmell, and Naira Baregamian

ACS CoC Cancer Liaison Physicians Meeting
10/19/2021
Disclosures

None
Papillary Thyroid Carcinoma (PTC)

- The most common endocrine malignancy
- Favorable overall prognosis for non-metastatic disease
- Tumor metastatic progression imparts dramatic reduction in 5-yr survival (~50%)
- Upregulated antioxidant system
- **Glutathione (GSH)** is enriched in PTCs
- Antioxidant enzymes, **Glutathione Peroxidases (GPXs)**, catalyze intracellular ROS and toxin neutralization by GSH.
- **Glutathione peroxidase 4 (GPX4)** regulates ferroptosis mediated cell death pathway in tumor cells.

Hypothesis

- Induction of ferroptosis by targeting GPX4 is critical to abrogate GSH cytoprotective and chemorresistant behaviors in TC cells \textit{in vitro}.
Methods

- **GPX4 Expression & Survival Analysis in human PTC:**
  1. **Computational Analysis** - TCGA Database (500 PTCs), TIMER2.0 software & cBioPortal

- **Targeting GPX4 & Ferroptosis Pathway in TC In Vitro Model:**
  1. **Human thyroid cancer cell lines (mutational signature)**
     - K1 (\(BRAF^{V600E}\) and \(PI3KCA\) mutant)
     - MDA-T32 (\(BRAF^{V600E}\) and TERT promoter mutant)
     - MDA-T68 (\(NRAS\) mutant and TERT promoter mutant)
     - Control – HThF, human thyroid fibroblasts
  2. **GPX4 and TfR1 expression** – qRT-PCR, Western blot
  3. **Pharmacologic inhibition of GPX4 with RSL3** – Western blot, immunofluorescence (IF), confocal microscopy, Brightfiled microscopy, ELISA, scratch test, CellTitrGLO
     - Ferroptosis pathway induction & lipid peroxidation
     - Tumor cell survival, spheroid formation, migration
     - Oxidative stress
     - Autophagy
     - DNA damage and damage repair response
     - mTOR signaling pathway
RESULTS: Enhanced GPX4 Expression in Thyroid Cancer

A

B

C

D

Graph A: Scatter plot showing GPX4 expression levels in various thyroid cancer samples compared to normal tissues. Each dot represents a sample, with color intensity indicating expression levels. Significant differences are marked with asterisks.

Graph B: Survival analysis showing the probability of survival over months. The graph compares normal GPX4 expression (light blue line) and GPX4 overexpression (red line). The p-value is 0.03.

Graph C: Bar graph illustrating relative mRNA expression levels of GPX4 and Tfr1 in different cell lines. Black bars represent HThF, red bars K1, blue bars MDA-T32, and green bars MDA-T68. GPX4 expression is highest in K1 and MDA-T32, while Tfr1 expression is highest in MDA-T68.

Graph D: Western blot analysis showing protein expression levels of GPX4 and GAPDH in HThF, K1, MDA-T32, and MDA-T68 cell lines. GPX4 expression is highest in K1 and MDA-T32, while GAPDH expression is consistent across all cell lines.
RESULTS: RSL3 Induces Ferroptosis and Rapid ROS Production in TC in vitro

A

DMSO

RSL3 (0.1 μM)

B

DMSO

RSL3 (μM)

0.25

0.50

1.0

2.0

3.0

TfR1

GAPDH

MDA-T32

C

DMSO

RSL3

BODIPY 581/591 C11

Low lipid peroxidation

High Lipid peroxidation

D

ROS Induction By RSL3

% Increase in ROS

1000

900

800

700

600

500

400

300

200

100

0

RSL3 Concentration (mM)
RESULTS: RSL3 Reduces Tumor Cell Viability, Impairs Spheroid Formation & Arrests Migration in TC in vitro
RESULTS: RSL3 Suppresses DNA Damage Repair Response & Activates Autophagy in TC *in vitro*
RESULTS: RSL3 Inhibits mTOR Pathway Signaling During Ferroptosis in TC in vitro

A

<table>
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<th>RSL3 (µM)</th>
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<tr>
<td>0.005</td>
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<td>0.01</td>
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<td>0.05</td>
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<td>0.1</td>
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p70S6K (total)
p-4E-BP1 (T37/46)
p-S6 (S235/236)
S6 (total)
GAPDH

B

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<th>RSL3 4 hr</th>
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p70S6K (total)
TfR1
GAPDH

C

DMSO

RSL3 (0.1 µM)

p70S6K

DAPI

DAPI p70S6K

D

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GPX4

p70S6K

γH2AX

LC3B I

LC3B II

β-actin

E

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<tr>
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<th>Ferrostatin-1</th>
<th>RSL-3</th>
<th>RSL-3 + Ferrostatin-1</th>
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p70S6K (total)
pS6 (S235/236)
pNPM1 (T199)
TfR1
GAPDH

F

DMSO

RSL3

Ferrostatin 1 + RSL3
Endocrine Neoplasia Laboratory – Baregamian Lab
Division of Surgical Oncology & Endocrine Surgery, Vanderbilt University Medical Center (VUMC)
- Naira Baregamian, MD, MMS, FACS (PI)
- Konjeti R. Sekhar, PhD (Staff Scientist)
- Sriram Cyr, BS (VUSM)

Collaborators
W. Kimryn Rathmell Lab - VUMC
- W. Kimryn Rathmell, MD, PhD (PI)

Ramesh Balusu Lab – U Kansas Medical Center
- Ramesh Balusu, PhD (PI)
- Sidhakiranmayi Kuravi, PhD (Staff Scientist)

Grant support (PI-Baregamian)
- Burroughs Wellcome Fund Vanderbilt SCRIPS Faculty Scholar Award
- NCI/VICC Multi-Tier Developmental Support Grant (P30CA068485)

Emails: david.n.hanna@vumc.org
naira.baregamian@vumc.org
Epigenetic Changes in Pancreatic Cancer (PDAC) with Pharmacologic Ascorbate (P-AscH⁻)

Garett J. Steers, MD; Brianne R. O’Leary, PhD; Juan Du, PhD; Rory S. Carrol, MD; Prabaht C. Goswami, PhD; Joseph J. Cullen, MD

From the Iowa City VAMC, University of Iowa Departments of Surgery, Radiation Oncology and Free Radical and Radiation Biology Program

Support: P01 CA217797 and T32 CA148062
DUOX1 methylation reduces patient survival in PDAC

- High methylation = decreased DUOX1 expression and decreased OS
- Decreased DUOX expression in vitro and in human pancreatic cancer
  
  Cancer Res. 2020 Apr 1;80(7):1401-1413

- DUOX expression is increased following pharmacologic ascorbate (P-AscH-) treatment
  
  Cancer Res. 2020 Apr 1;80(7):1401-1413
DNA Methylation/Demethylation of Cytosine Bases

- DNA Methyltransferase (DNMT) increases DNA methylation.
- DNMT1 expression increased under hypoxia.
- Ten-eleven translocation enzyme (TET) decreases DNA methylation.
- Promoter methylation = decreased downstream gene expression.
- Required TET cofactor: ascorbate
Hypothesis

• DUOX enzymes are epigenetically silenced in pancreatic cancer (PDAC), and increasing their expression may increase $\text{H}_2\text{O}_2$ production, decrease cancer cell growth, and improve survival.
5-AZD and 5-AZC increase expression of DUOX1 & DUOX2

MIA PaCa-2

DUOX1 mRNA Expression

Control
P-AscH
0.5µM 5-AZD
1µM 5-AZD
0.5µM 5-AZD+P-AscH
1µM 5-AZD+P-AscH

10 pmole/cell P-AscH
*p < 0.05, n=3

MIA PaCa-2

DUOX2 mRNA Expression

Control
P-AscH
0.5µM 5-AZD
1µM 5-AZD
0.5µM 5-AZD+P-AscH
1µM 5-AZD+P-AscH

339

DUOX1

Tubulin

Commission on Cancer 2021
P-AscH\(^-\) & 5-AZC increase H\(_2\)O\(_2\)

20 pmole/cell P-AscH\(^-\)
2 \(\mu\)M 5-AZC

\(* \ p < 0.05, n=3\)
5-AZD + P-AscH⁻ reduces clonogenic survival

PANC-1

20 pmole/cell P-AscH⁻
* p < 0.0001, n=3

Clonogenic Survival

Control
P-AscH⁻
0.1µM 5-AZD
0.1µM 5-AZD+P-AscH⁻
P-AscH⁻ decreases DNMT1 expression in hypoxia

**Graph:**
- **X-axis:** Control, P-AscH⁻, 6h Hypoxia, 6h Hypoxia+P-AscH⁻
- **Y-axis:** DNMT1 Expression

**Legend:**
- MIA PaCa-2
- Control, P-AscH⁻, 6h Hypoxia, 6h Hypoxia+P-AscH⁻

**Statistical Data:**
- 10 pmole/cell P-AscH⁻
- ∗ p < 0.05, n=3
5-AZD + P-AscH\(^{-}\) reduces tumor volume \textit{in vivo}\n
\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{tumor_volume_progression.png}
\caption{Tumor Volume Progression}
\end{figure}

- **Control**
- **P-AscH\(^{-}\)**
- **5-AZD**
- **P-AscH\(^{-}\)+5-AZD**

1M saline daily
4g/kg P-AscH\(^{-}\) daily
1g/kg 5-AZD 3x weekly

\(* p < 0.001\)
Conclusions

• DNMT inhibitors increase DUOX1 and DUOX2 expression in PDAC.

• P-AscH⁻ enhances the cytotoxic and epigenetic effects of DNMT inhibitors through a \( \text{H}_2\text{O}_2 \) mechanism.

• P-AscH⁻ decreases DNMT1 expression in hypoxia.

• DNMT inhibitors act synergistically with P-AscH⁻ to decrease tumor volume in a xenograft model of PDAC.

• DNMT inhibitors, in combination with P-AscH⁻, have the potential to sensitize PDAC to chemotherapy.
Please enter your questions in the Questions section.
Thank you!

Staff Liaisons:
Melissa Leeb mleeb@facs.org
Danielle Lopez dlopez@facs.org