# Finding New Immunotherapy Targets in Osteosarcoma

Busra Turgu[1,2], Amal M. EL-Naggar[1,2], Sandra Spencer[3], Gian Luca Negri[3], Andri Konstantinou[4], Anna Obenauf[4], Alejandro Sweet-Cordero[5], Gregg Morin[3], Poul Sorensen[1,2]*

1. Department of Molecular Oncology, BC Cancer Research Institute, Vancouver, BC, Canada
2. Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada
3. Michael Smith Genome Sciences Centre, BC Cancer Research Institute, Vancouver, BC, Canada
4. Research Institute of Molecular Pathology (IMP), Vienna, Austria
5. Department of Pediatrics, University of California San Francisco, San Francisco, California.

## Introduction

- Osteosarcoma (OS) is the most common bone cancer in young adults.
- The standard of care for OS is limited to chemotherapy and surgery, which have significant side effects and a high recurrence rate. Furthermore, refractory OS remains largely incurable, highlighting a critical unmet need.
- Immunotherapy (IT) has emerged as a promising alternative, offering long-term therapeutic benefits through durable responses and immune memory.
- The success of IT in OS remains limited due to the lack of known tumor-specific surface antigens.

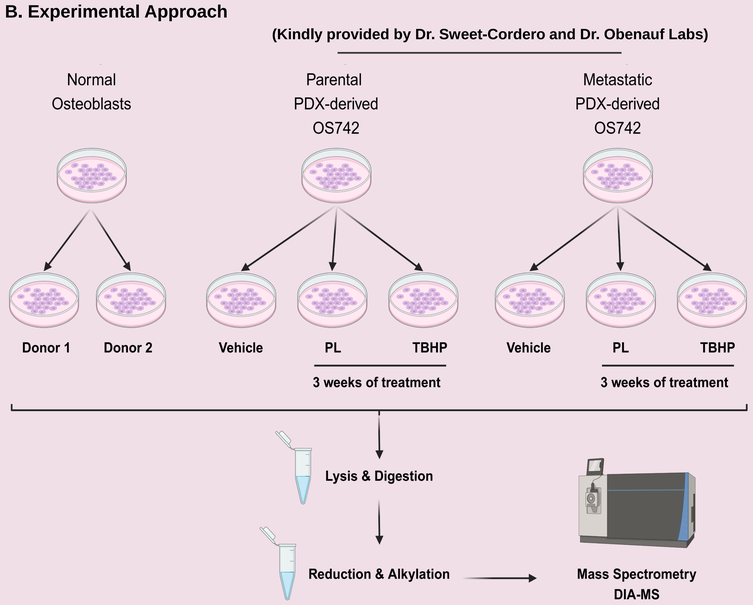
## Objective

- This study aims to identify novel OS-specific immunotherapy targets by analyzing differentially expressed surface proteins in PDX-derived OS cells under ambient conditions and oxidative stress, one of the major stressors in the physiological tumor microenvironment.

## Experimental Design

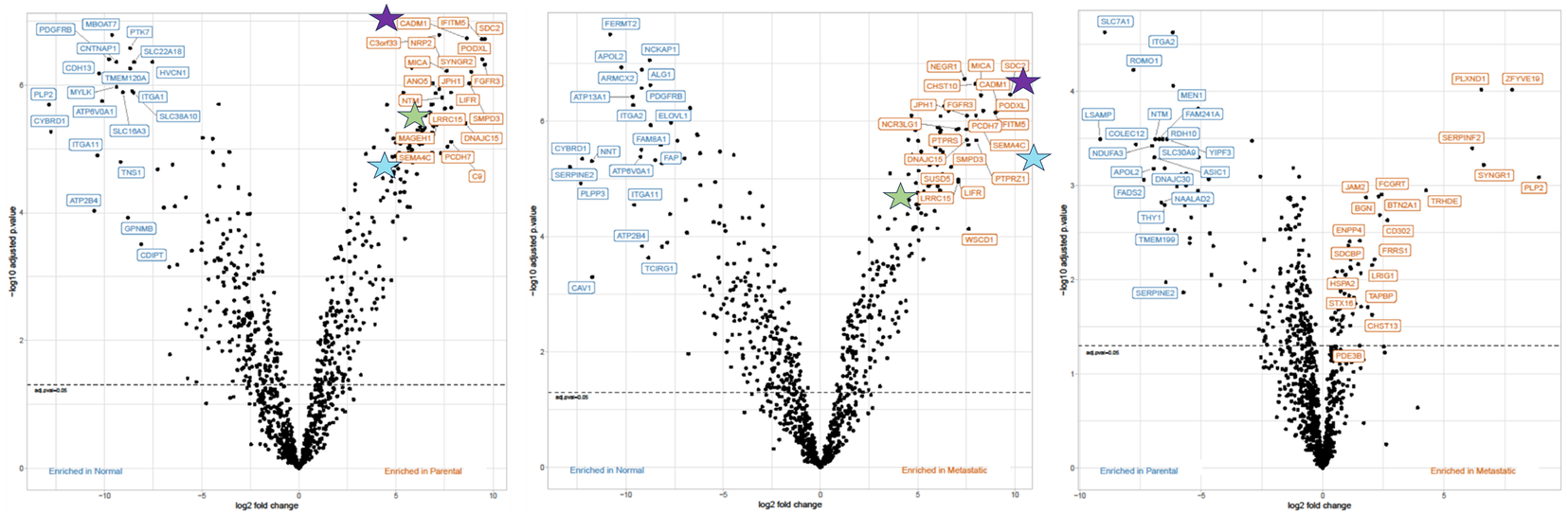
**A. Cell Lines: Established Normal Osteoblasts, Patient-Derived Parental Osteosarcoma, and Metastatic Osteosarcoma Cell Lines Derived from Parental PDXs**

**B. Experimental Approach**




## RESULTS

**Differential Expression of Surface Proteins in Normal Osteoblasts and Osteosarcoma**




> Oncogene. 2020 Jan;39(5):1049-1062. doi: 10.1038/s41388-019-1041-x. Epub 2019 Oct 3.

**SEMA4C is a novel target to limit osteosarcoma growth, progression, and metastasis**

Branden A Smeester [1 2 3], Nicholas J Slipek [1 2 3], Emily J Pomeroy [1 2 3], Heather E Bomberger [4], Ghaidan A Shamsan [3 4], Joseph J Peterson [1 2 3], Margaret R Crosby [1 2 3], Garrett M Draper [1 2 3], Kelsie L Becklin [1 2 3], Eric P Rahrmann [5], James B McCarthy [3 6], David J Odde [3 4], David K Wood [4], David A Largaespada [1 2 3], Branden S Moriarity [7 8 9]

Affiliations + expand

PMID: 31582836 DOI: 10.1038/s41388-019-1041-x

> Pediatr Blood Cancer. 2021 Feb;68(2):e28771. doi: 10.1002/pbc.28771. Epub 2020 Oct 16.

**LRRC15 antibody-drug conjugates show promise as osteosarcoma therapeutics in preclinical studies**

Katherine K Slemmons [1], Sanjit Mukherjee [2], Paul Meltzer [2], James W Purcell [3], Lee J Helman [1 4]

Affiliations + expand

PMID: 33063919 PMCID: PMC9137401 DOI: 10.1002/pbc.28771

> Life Sci. 2013 Jan 17;92(1):91-9. doi: 10.1016/j.lfs.2012.10.021. Epub 2012 Nov 7.

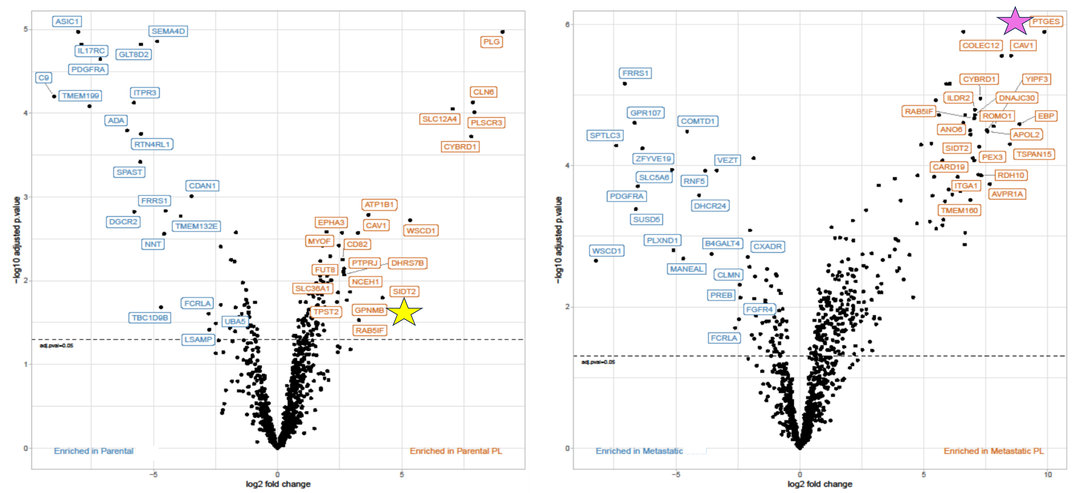
**Cell adhesion molecule 1 is a new osteoblastic cell adhesion molecule and a diagnostic marker for osteosarcoma**

Takao Inoue [1], Man Hagiyama, Eisuke Enoki, Minami A Sakurai, Akihiro Tan, Tomohiko Wakayama, Shoichi Iseki, Yoshinori Murakami, Kanji Fukuda, Chiaki Hamanishi, Akihiko Ito

Affiliations + expand

PMID: 23142238 DOI: 10.1016/j.lfs.2012.10.021

**Differential Expression of Surface Proteins in Response to Piperlongamine (PL) Treatment**




CELL, TUMOR, AND STEM CELL BIOLOGY | AUGUST 15 2007

**Caveolin-1 Reduces Osteosarcoma Metastases by Inhibiting c-Src Activity and Met Signaling** FREE

Lara Cantiani; Maria Cristina Manara; Cinzia Zucchini; Paola De Sanctis; Monia Zuntini; Luisa Valvassori; Massimo Serra; Martina Olivero; Maria Flavia Di Renzo; Mario Paolo Colombo; Piero Picci; Katia Scotlandi

Check for updates

Author & Article Information

*Cancer Res* (2007) 67 (16): 7675–7685.

https://doi.org/10.1158/0008-5472.CAN-06-4697 **Article history**

Eur J Cancer. Author manuscript; available in PMC: 2020 Oct 31.

*Published in final edited form as:* Eur J Cancer. 2019 Oct 3;121:177–183. doi: 10.1016/j.ejca.2019.08.015

**Phase 2 Trial of the GPNMB-Targeted Antibody-Drug Conjugate, Glembatumumab Vedotin (CDX-011) in Recurrent Osteosarcoma AOST1521: A Report from the Children's Oncology Group (COG)**

Lisa M Kopp [1,2], Suman Malempati [3], Mark Krailo [4,5], Yun Gao [4], Allen Buxton [4], Brenda J Weigel [6], Thomas Hawthorne [7], Elizabeth Crowley [7], Jeffrey A Moscow [8], Joel M Reid [9], Victor Villalobos [10], R Lor Randall [11], Richard Gorlick [12], Katherine A Janeway [13]

Author information Article notes Copyright and License information

PMCID: PMC6952063 NIHMSID: NIHMS1547420 PMID: 31586757

## Next Steps

1) Prioritize immunotherapy targets based on:
- ➢ High and homogeneous expression in cancer
- ➢ Minimal expression in normal healthy tissues
- ➢ Functional relevance to the tumor
- ➢ Available extracellular residues

2) Experimental validation of the selected targets
- Functional studies
- In vitro and in vivo validation

3) Development of immunotherapies such as antibody-drug conjugates (ADCs) or CAR-T cell therapy to the selected cancer-specific target.

Alex's Lemonade Stand Foundation for Childhood Cancer™