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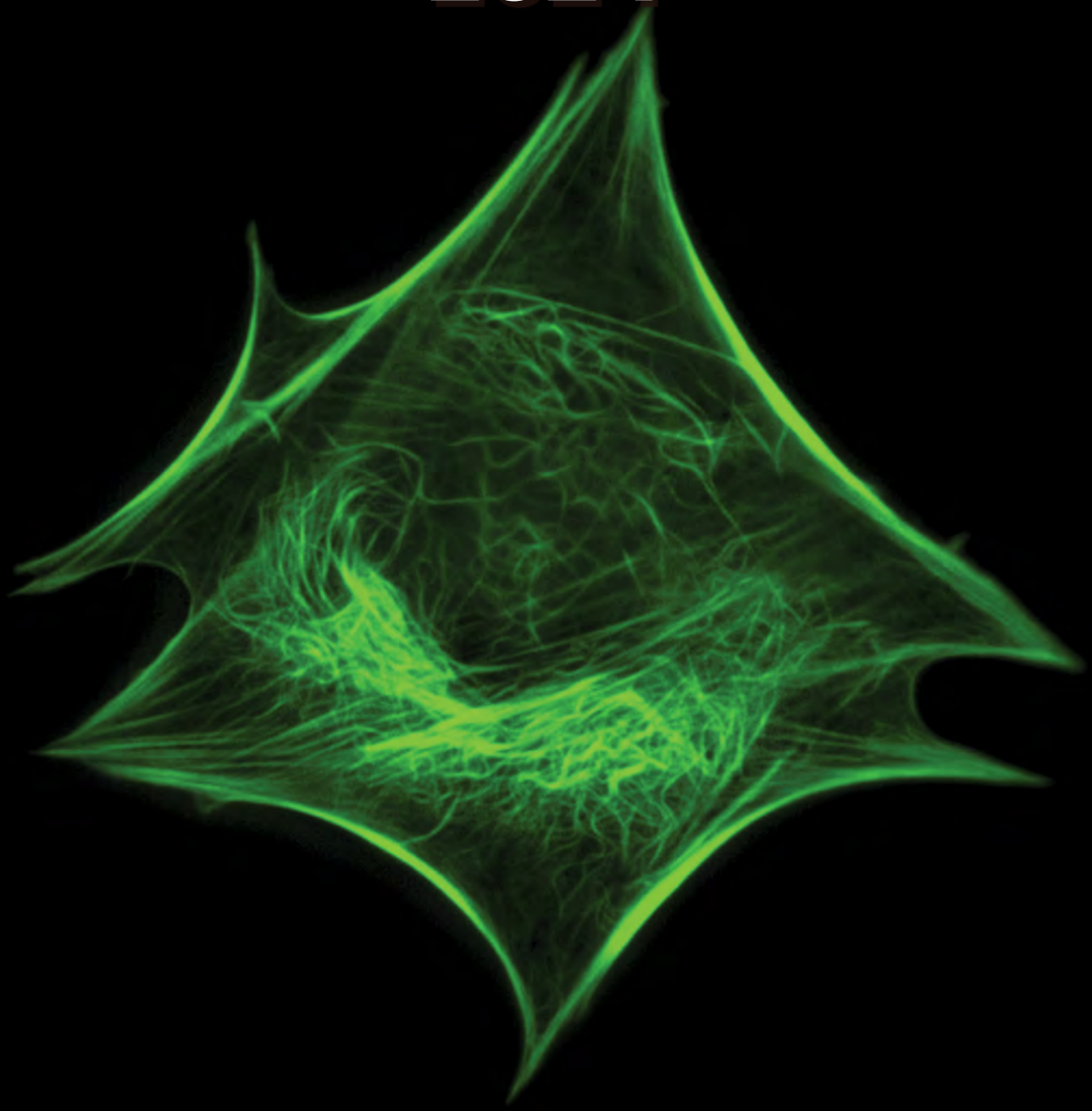

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Brochure articles by Ben Short, PhD

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On the cover: Image shows the organization of actin in a breast cancer cell under low oxygen conditions.

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A CANCER-ASSOCIATED EXON ALTERS TALIN-1 MECHANOSENSITIVITY AND CELL MOTILITY

Talin-1 is the core mechanosensitive adapter protein linking integrins to the cytoskeleton. The *TLN1* gene is comprised of 57 exons that encode the 2,541 amino acid TLN1 protein. TLN1 was previously considered to be expressed as a single isoform. However, through differential pre-mRNA splicing analysis, we discovered a cancer-enriched, non-annotated 51-nucleotide exon in *TLN1* between exons 17 and 18, which we refer to as exon 17b.

TLN1 is comprised of an N-terminal FERM domain, linked to 13 force-dependent switch domains, R1-R13. Inclusion of exon 17b introduces an in-frame insertion of 17 amino acids immediately after Gln665 in the region between R1 and R2, which lowers the force required to open the R1-R2 switches potentially altering downstream mechanotransduction.

Biochemical analysis of this isoform revealed enhanced vinculin binding, and cells expressing this variant show altered adhesion dynamics and motility. Finally, we showed that the TGF-β/SMAD3 signaling pathway regulates this isoform switch. Future studies will need to consider the balance of these two TLN1 isoforms.

ORIGINAL PAPER

Gallego-Paez, L.M., W.J.S. Edwards, M. Chanduri, Y. Guo, T. Koorman, C.-Y. Lee, N. Grexa, P. Derksen, J. Yan, M.A. Schwartz, J. Mauer, and B.T. Goult. 2023. *TLN1* contains a cancer-associated cassette exon that alters talin-1 mechanosensitivity. *J. Cell Biol.* 222 (5): e202209010. https://doi.org/10.1083/jcb.202209010

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PIM1 KINASE DRIVES HYPOXIA-INDUCED PROSTATE CANCER CELL INVASION

Distinguishing key factors that drive the switch from indolent to invasive disease will make a significant impact on guiding the treatment of prostate cancer (PCa) patients. We identified a novel signaling pathway linking hypoxia and PIM1 kinase to the actin cytoskeleton and cell motility.

An unbiased proteomic screen identified Abl-interactor 2 (ABI2), an integral member of the wave regulatory complex (WRC), as a PIM1 substrate. Phosphorylation of ABI2 at Ser183 by PIM1 increased ABI2 protein levels and enhanced WRC formation, resulting in increased protrusive activity and cell motility. Cell protrusion induced by hypoxia and/or PIM1 was dependent on ABI2.

In vivo smooth muscle invasion assays showed that overexpression of PIM1 significantly increased the depth of tumor cell invasion, and treatment with PIM inhibitors significantly reduced intramuscular PCa invasion. This research uncovers a HIF-1-independent signaling axis that is critical for hypoxia-induced invasion and establishes a novel role for PIM1 as a key regulator of the actin cytoskeleton.

ORIGINAL PAPER

Jensen, C.C., A.N. Clements, H. Liou, L.E. Ball, J.R. Bethard, P.R. Langlais, R.K. Toth, S.S. Chauhan, A.L. Casillas, S.R. Daulat, A.S. Kraft, A.E. Cress, C.K. Miranti, G. Mouneimne, G.C. Rogers, and N.A. Warfel. 2023. PIM1 phosphorylates ABI2 to enhance actin dynamics and promote tumor invasion. *J. Cell Biol.* 222 (6): e202208136. https://doi.org/10.1083/jcb.202208136

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B CELL LYMPHOMAS MAY BE VULNERABLE TO INHIBITORS OF PHOSPHATIDYLSERINE SYNTHESIS

Cancer cells harness lipid metabolism to promote their own survival. We screened 47 cancer cell lines for survival dependency on phosphatidylserine (PS) synthesis using a PS synthase 1 (PTDSS1) inhibitor and found that B cell lymphoma is highly dependent on PS.

Inhibition of PTDSS1 in B cell lymphoma cells caused a reduction of PS and phosphatidylethanolamine levels and an increase of phosphoinositide levels. The resulting imbalance of the membrane phospholipidome lowered the activation threshold for B cell receptor (BCR), a B cell–specific survival mechanism. BCR hyperactivation led to aberrant elevation of downstream Ca^{2+} signaling and subsequent apoptotic cell death. In a mouse xenograft model, PTDSS1 inhibition efficiently suppressed tumor growth and prolonged survival.

Our findings suggest that PS synthesis may be a critical vulnerability of malignant B cell lymphomas that can be targeted pharmacologically.

ORIGINAL PAPER

Omi, J., T. Kato, Y. Yoshihama, K. Sawada, N. Kono, and J. Aoki. 2024. Phosphatidylserine synthesis controls oncogenic B cell receptor signaling in B cell lymphoma. *J. Cell Biol.* 223 (2): e202212074. https://doi.org/10.1083/jcb.202212074

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MELANOMA CELLS ENHANCE THEIR MIGRATION BY REPRESSING A KERATINOCYTE ADHESION MOLECULE

Melanoma is an aggressive cancer typically arising from transformation of melanocytes residing in the basal layer of the epidermis, where they are in direct contact with surrounding keratinocytes. The role of keratinocytes in shaping the melanoma tumor microenvironment remains understudied.

We previously showed that temporary loss of the keratinocyte-specific cadherin, Desmoglein 1 (Dsg1), controls paracrine signaling between normal melanocytes and keratinocytes to stimulate the protective tanning response. Here, we provide evidence that melanoma cells hijack this intercellular communication by secreting factors that keep Dsg1 expression low in the surrounding keratinocytes, which in turn generate their own paracrine signals that enhance melanoma spread through CXCL1/CXCR2 signaling. Evidence suggests a model whereby paracrine signaling from melanoma cells increases levels of the transcriptional repressor Slug, and consequently decreases expression of the Dsg1 transcriptional activator Grhl1.

Together, these data support the idea that paracrine crosstalk between melanoma cells and keratinocytes resulting in chronic keratinocyte Dsg1 reduction contributes to melanoma cell movement associated with tumor progression.

ORIGINAL PAPER

Burks, H.E., J.L. Pokorny, J.L. Koetsier, Q.R. Roth-Carter, C.R. Arnette, P. Gerami, J.T. Seykora, J.L. Johnson, Z. Ren, and K.J. Green. Melanoma cells repress Desmoglein 1 in keratinocytes to promote tumor cell migration. 2023. *J. Cell Biol.* 222 (11): e202212031. https://doi.org/10.1083/jcb.202212031

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TGF-β-INDUCED HER2 PHOSPHORYLATION PROMOTES BREAST CANCER PROGRESSION

Transforming growth factor β (TGF-β) and HER2 signaling collaborate to promote breast cancer progression. However, their molecular interplay is largely unclear. TGF-β can activate mitogen-activated protein kinase (MAPK) and AKT, but the underlying mechanism is not fully understood.

In this study, we report that TGF-β enhances HER2 activation, leading to the activation of MAPK and AKT. This process depends on the TGF-β type I receptor TβRI kinase activity. TβRI phosphorylates HER2 at Ser779, promoting Y1248 phosphorylation and HER2 activation. Mice with HER2 S779A mutation display impaired mammary morphogenesis, reduced ductal elongation, and branching. Furthermore, wild-type HER2, but not S779A mutant, promotes TGF-β-induced epithelial–mesenchymal transition, cell migration, and lung metastasis of breast cells. Increased HER2 S779 phosphorylation is observed in human breast cancers and positively correlated with the activation of HER2, MAPK, and AKT.

Our findings demonstrate the crucial role of TGF-β-induced S779 phosphorylation in HER2 activation, mammary gland development, and the pro-oncogenic function of TGF-β in breast cancer progression.

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ORIGINAL PAPER
Shi, Q., F. Huang, Y. Wang, H. Liu, H. Deng, Y.-G. Chen. 2024. HER2 phosphorylation induced by TGF-β promotes mammary morphogenesis and breast cancer progression. *J. Cell Biol.* 223 (4): e202307138. https://doi.org/10.1083/jcb.202307138

EML4-ALK DRIVES LUNG ADENO-TO-SQUAMOUS TRANSITION

Human lung adenosquamous cell carcinoma (LUAS), containing both adenomatous and squamous pathologies, exhibits strong cancer plasticity. We find that ALK rearrangement is detectable in 5.1–7.5% of human LUAS, and transgenic expression of EML4-ALK drives lung adenocarcinoma (LUAD) formation initially and squamous transition at late stage.

We identify club cells as the main cell of origin for squamous transition. By recapitulating lineage transition in an organoid system, we identify that JAK-STAT signaling, activated by EML4-ALK phase separation, significantly promotes squamous transition. Integrative study with scRNA-seq and immunostaining identify a plastic cell subpopulation in ALK-rearranged human LUAD showing squamous biomarker expression. Moreover, those relapsed ALK-rearranged LUAD show notable upregulation of squamous biomarkers. Consistently, mouse squamous tumors or LUAD with squamous signature display certain resistance to ALK inhibitor, which can be overcome by combined JAK1/2 inhibitor treatment.

This study uncovers strong plasticity of ALK-rearranged tumors in orchestrating phenotypic transition and drug resistance and proposes a potentially effective therapeutic strategy.

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Qin, Z., M. Yue, S. Tang, F. Wu, H. Sun, Y. Li, Y. Zhang, H. Izumi, H. Huang, W. Wang, Y. Xue, X. Tong, S. Mori, T. Taki, K. Goto, Y. Jin, F. Li, F.-M. Li, Y. Gao, Z. Fang, Y. Fang, L. Hu, X. Yan, G. Xu, H. Chen, S.S. Kobayashi, A. Ventura, K.-K. Wong, X. Zhu, L. Chen, S. Ren, L.-N. Chen, and H. Ji. EML4-ALK fusions drive lung adeno-to-squamous transition through JAK-STAT activation. 2024. *J. Exp. Med.* 221 (3): e20232028. https://doi.org/10.1084/jem.20232028

CLONAL HEMATOPOIESIS PROMOTES COLON CANCER

Clonal hematopoiesis (CH) is defined as clonal expansion of mutant hematopoietic stem cells absent diagnosis of a hematologic malignancy. Presence of CH in solid tumor patients, including colon cancer, correlates with shorter survival. We hypothesized that bone marrow–derived cells with heterozygous loss-of-function mutations of *DNMT3A*, the most common genetic alteration in CH, contribute to the pathogenesis of colon cancer.

In a mouse model that combines colitis-associated colon cancer (CAC) with experimental CH driven by *Dnmt3a+/Δ*, we found higher tumor penetrance and increased tumor burden compared with controls. Histopathological analysis revealed accentuated colonic epithelium injury, dysplasia, and adenocarcinoma formation. Transcriptome profiling of colon tumors identified enrichment of gene signatures associated with carcinogenesis, including angiogenesis. Treatment with the angiogenesis inhibitor axitinib eliminated the colon tumor-promoting effect of experimental CH driven by *Dnmt3a* haploinsufficiency and rebalanced hematopoiesis.

This study provides conceptually novel insights into non-tumor-cell-autonomous effects of hematopoietic alterations on colon carcinogenesis and identifies potential therapeutic strategies.

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ORIGINAL PAPER
Feng, Y., Q. Yuan, R.C. Newsome, T. Robinson, R.L. Bowman, A.N. Zuniga, K.N. Hall, C.M. Bernsten, D.E. Shabashvili, K.I. Krajcik, C. Gunaratne, Z.J. Zaroogian, K. Venugopal, H.L. Casellas Roman, R.L. Levine, W.K. Chatila, R. Yaeger, A. Riva, C. Jobin, D. Kopinke, D. Avram, and O.A. Guryanova. 2023. Hematopoietic-specific heterozygous loss of *Dnmt3a* exacerbates colitis-associated colon cancer. *J. Exp. Med.* 220 (11): e20230011. https://doi.org/10.1084/jem.20230011

JEM Journal of Experimental Medicine

E-CADHERIN LOSS PROMOTES TRANSCRIPTIONAL REPROGRAMMING AND IMMUNE EVASION IN DGAC

Diffuse-type gastric adenocarcinoma (DGAC) is a deadly cancer often diagnosed late and resistant to treatment. While hereditary DGAC is linked to *CDH1* mutations, the role of CDH1/E-cadherin inactivation in sporadic DGAC tumorigenesis remains elusive.

We discovered CDH1 inactivation in a subset of DGAC patient tumors. Analyzing single-cell transcriptomes in malignant ascites, we identified two DGAC subtypes: DGAC1 (CDH1 loss) and DGAC2 (lacking immune response). DGAC1 displayed distinct molecular signatures, activated DGAC-related pathways, and an abundance of exhausted T cells in ascites. Genetically engineered murine gastric organoids showed that *Cdh1* knock-out (KO), *KrasG12D*, *Trp53* KO (EKP) accelerates tumorigenesis with immune evasion compared with *KrasG12D*, *Trp53* KO (KP). We also identified EZH2 as a key mediator promoting CDH1 loss-associated DGAC tumorigenesis.

These findings highlight DGAC's molecular diversity and potential for personalized treatment in CDH1-inactivated patients.

ORIGINAL PAPER

Zou, G., Y. Huang, S. Zhang, K.-P. Ko, B. Kim, J. Zhang, V. Venkatesan, M.P. Pizzi, Y. Fan, S. Jun, N. Niu, H. Wang, S. Song, J.A. Ajani, and J.-I. Park. 2024. E-cadherin loss drives diffuse-type gastric tumorigenesis via EZH2-mediated reprogramming. *J. Exp. Med.* 221 (4): e20230561. https://doi.org/10.1084/jem.20230561

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MHC-II⁺ BREAST CANCER CELLS PROMOTE IMMUNE TOLERANCE AND METASTASIS

Tumor-draining lymph nodes (TDLNs) are important for tumor antigen–specific T cell generation and effective anticancer immune responses. However, TDLNs are often the primary site of metastasis, causing immune suppression and worse outcomes. Through cross-species single-cell RNA-Seq analysis, we identified features defining cancer cell heterogeneity, plasticity, and immune evasion during breast cancer progression and lymph node metastasis (LNM).

A subset of cancer cells in the lymph nodes exhibited elevated MHC class II (MHC-II) gene expression in both mice and humans. MHC-II⁺ cancer cells lacked costimulatory molecule expression, leading to regulatory T cell (Treg) expansion and fewer CD4⁺ effector T cells in TDLNs. Genetic knockout of MHC-II reduced LNM and Treg expansion, while overexpression of the MHC-II transactivator, *Ciita*, worsened LNM and caused excessive Treg expansion.

These findings demonstrate that cancer cell MHC-II expression promotes metastasis and immune evasion in TDLNs.

ORIGINAL PAPER

Lei, P.J., E.R. Pereira, P. Andersson, Z. Amoozgar, J.W. Van Wijnbergen, M.J. O'Melia, H. Zhou, S. Chatterjee, W.W. Ho, J.M. Posada, A.S. Kumar, S. Morita, L. Menzel, C. Chung, I. Ergin, D. Jones, P. Huang, S. Beyaz, and T.P. Padera. 2023. Cancer cell plasticity and MHC-II–mediated immune tolerance promote breast cancer metastasis to lymph nodes. *J. Exp. Med.* 220 (9): e20221847. https://doi.org/10.1084/jem.20221847

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MACROPHAGE PROLIFERATION DRIVES PDAC PROGRESSION AND IMMUNOTHERAPY SUSCEPTIBILITY

Tumor-associated macrophages (TAMs) are abundant in pancreatic ductal adenocarcinomas (PDACs). While TAMs are known to proliferate in cancer tissues, the impact of this on macrophage phenotype and disease progression is poorly understood.

We showed that in PDAC, proliferation of TAMs could be driven by colony stimulating factor-1 (CSF1) produced by cancer-associated fibroblasts. CSF1 induced high levels of p21 in macrophages, which regulated both TAM proliferation and phenotype. TAMs in human and mouse PDACs with high levels of p21 had more inflammatory and immunosuppressive phenotypes.

p21 expression in TAMs was induced by both stromal interaction and/or chemotherapy treatment. Finally, by modeling p21 expression levels in TAMs, we found that p21-driven macrophage immunosuppression in vivo drove tumor progression. Serendipitously, the same p21-driven pathways that drive tumor progression also drove response to CD40 agonist.

These data suggest that stromal or therapy-induced regulation of cell cycle machinery can regulate both macrophage-mediated immune suppression and susceptibility to innate immunotherapy.

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ORIGINAL PAPER
Zuo, C., J.M. Baer, B.L. Knolhoff, J.I. Belle, X. Liu, A.A. De La Lastra, C. Fu, G.D. Hogg, N.L. Kingston, M.A. Breden, P.B. Dodhiawala, D.C. Zhou, V.E. Lander, C.A. James, L. Ding, K.-H. Lim, R.C. Fields, W.G. Hawkins, J.D. Weber, G. Zhao, and D.G. DeNardo. 2023. Stromal and therapy-induced macrophage proliferation promotes PDAC progression and susceptibility to innate immunotherapy. *J. Exp. Med.* 220 (6): e20212062. https://doi.org/10.1084/jem.20212062

Life Science Alliance

TARGETING CHRONIC LYMPHOCYTIC LEUKEMIA WITH A SPLICING FACTOR INHIBITOR

Splicing factor 3B subunit 1 (SF3B1) is involved in pre-mRNA branch site recognition and is the target of antitumor-splicing inhibitors. Mutations in *SF3B1* are observed in 15% of patients with chronic lymphocytic leukemia (CLL) and are associated with poor prognosis, but their pathogenic mechanisms remain poorly understood.

Using deep RNA-sequencing data from 298 CLL tumor samples and isogenic *SF3B1* WT and K700E-mutated CLL cell lines, we characterize targets and pre-mRNA sequence features associated with the selection of cryptic 3′ splice sites upon *SF3B1* mutation, including an event in the *MAP3K7* gene relevant for activation of NF-κB signaling.

Using the H3B-8800 splicing modulator, we show, for the first time in CLL, cytotoxic effects in vitro in primary CLL samples and in *SF3B1*-mutated isogenic CLL cell lines, accompanied by major splicing changes and delayed leukemic infiltration in a CLL xenotransplant mouse model. H3B-8800 displayed preferential lethality towards *SF3B1*-mutated cells and synergism with the BCL2 inhibitor venetoclax, supporting the potential use of SF3B1 inhibitors as a novel therapeutic strategy in CLL.

ORIGINAL PAPER

López-Oreja, I., A. Gohr, H. Playa-Albinyana, A. Giró, F. Arenas, M. Higashi, R. Tripathi, M. López-Guerra, M. Irimia, M. Aymerich, J. Valcárcel, S. Bonnal, and D. Colomer. 2023. *SF3B1* mutation–mediated sensitization to H3B-8800 splicing inhibitor in chronic lymphocytic leukemia. *Life Science Alliance*. 6 (11): e202301955. https://doi.org/10.26508/lsa.202301955

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SPT5 DEPLETION INHIBITS MYC-DRIVEN TUMOR GROWTH IN FLIES

The transcription factor SPT5 physically interacts with MYC oncoproteins and is essential for efficient transcriptional activation of MYC targets in cultured cells. We used *Drosophila* to address the relevance of this interaction in a living organism.

Spt5 displays moderate synergy with Myc in fast proliferating young imaginal disc cells. During later development, Spt5-knockdown has no detectable consequences on its own, but strongly enhances eye defects caused by Myc overexpression. Similarly, Spt5-knockdown in larval type 2 neuroblasts has only mild effects on brain development and survival of control flies, but dramatically shrinks the volumes of experimentally induced neuroblast tumors and significantly extends the lifespan of tumor-bearing animals.

This beneficial effect is still observed when Spt5 is knocked down systemically and after tumor initiation, highlighting SPT5 as a potential drug target in human oncology.

ORIGINAL PAPER

Hofstetter, J., A. Ogunleye, A. Kutschke, L.M. Buchholz, E. Wolf, T. Raabe, and P. Gallant. 2023. Spt5 interacts genetically with Myc and is limiting for brain tumor growth in *Drosophila*. *Life Science Alliance*. 7 (1): e202302130. https://doi.org/10.26508/lsa.202302130

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A SRC-NRF2 AXIS RESISTS RADIATION-INDUCED FERROPTOSIS IN GLIOBLASTOMA

Glioblastoma is a severe brain tumor characterized by an extremely poor survival rate of patients. Glioblastoma cancer cells escape to standard therapeutic protocols consisting of a combination of ionizing radiation and temozolomide alkylating drugs that trigger DNA damage by rewiring of signaling pathways. In recent years, the up-regulation of factors that counteract ferroptosis has been highlighted as a major driver of cancer resistance to ionizing radiation, although the molecular connection between the activation of oncogenic signaling and the modulation of ferroptosis has not been clarified yet.

We provide the first evidence for a molecular connection between the constitutive activation of tyrosine kinases and resistance to ferroptosis. Src tyrosine kinase, a central hub on which deregulated receptor tyrosine kinase signaling converge in cancer, leads to the stabilization and activation of NRF2 pathway, thus promoting resistance to ionizing radiation–induced ferroptosis.

These data suggest that the up-regulation of the Src–NRF2 axis may represent a vulnerability for combined strategies that, by targeting ferroptosis resistance, enhance radiation sensitivity in glioblastoma.

ORIGINAL PAPER

Cirotti, C., I. Taddei, C. Contadini, C. Di Girolamo, G. Pepe, M. De Bardi, G. Borsellino, M. Helmer-Citterich, and D. Barilà. 2023. NRF2 connects Src tyrosine kinase to ferroptosis resistance in glioblastoma. *Life Science Alliance.* 7 (1): e202302205. https://doi.org/10.26508/lsa.202302205

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THE MITOCHONDRIAL PROTEASE OMA1 REDUCES SARCOMA IMMUNOGENICITY

Aggressive tumors often display mitochondrial dysfunction. Upon oxidative stress, mitochondria undergo fission through OMA1-mediated cleavage of the fusion effector OPA1. In yeast, a redox-sensing switch participates in OMA1 activation. 3D modeling of OMA1 comforted the notion that cysteine 403 might participate in a similar sensor in mammalian cells.

Using prime editing, we developed a mouse sarcoma cell line in which OMA1 cysteine 403 was mutated to alanine. Mutant cells showed impaired mitochondrial responses to stress including ATP production, reduced fission, resistance to apoptosis, and enhanced mitochondrial DNA release. This mutation prevented tumor development in immunocompetent, but not nude or cDC1 dendritic cell–deficient, mice. These cells prime $CD8^+$ lymphocytes that accumulate in mutant tumors, whereas their depletion delays tumor control. Thus, OMA1 inactivation increased the development of anti-tumor immunity.

Patients with complex genomic soft tissue sarcoma showed variations in the level of OMA1 and OPA1 transcripts. High expression of OPA1 in primary tumors was associated with shorter metastasis-free survival after surgery, and low expression of OPA1, with anti-tumor immune signatures. Targeting OMA1 activity may enhance sarcoma immunogenicity.

ORIGINAL PAPER

Miallot, R., V. Millet, Y. Groult, A. Modelska, L. Crescence, S. Roulland, S. Henri, B. Malissen, N. Brouilly, L. Panicot-Dubois, R. Vincentelli, G. Sulzenbacher, P. Finetti, A. Dutour, J.-Y. Blay, F. Bertucci, F. Galland, and P. Naquet. 2023. An OMA1 redox site controls mitochondrial homeostasis, sarcoma growth, and immunogenicity. *Life Science Alliance.* 6 (6): e202201767. https://doi.org/10.26508/lsa.202201767

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THE THIOL-REACTIVE COMPOUND APR-246 ENHANCES TUMOR IMMUNOGENICITY

We previously reported that activation of p53 by APR-246 reprograms tumor-associated macrophages to overcome immune checkpoint blockade resistance. Here, we demonstrate that APR-246 and its active moiety, methylene quinuclidinone (MQ) can enhance the immunogenicity of tumor cells directly.

MQ treatment of murine B16F10 melanoma cells promoted activation of melanoma-specific $CD8^+$ T cells and increased the efficacy of a tumor cell vaccine using MQ-treated cells even when the B16F10 cells lacked p53. We then designed a novel combination of APR-246 with the TLR-4 agonist, monophosphoryl lipid A, and a CD40 agonist to further enhance these immunogenic effects and demonstrated a significant antitumor response.

We propose that the immunogenic effect of MQ can be linked to its thiol-reactive alkylating ability, as we observed similar immunogenic effects with the broad-spectrum cysteine-reactive compound, iodoacetamide. Our results thus indicate that combination of APR-246 with immunomodulatory agents may elicit effective antitumor immune response irrespective of the tumor's p53 mutation status.

ORIGINAL PAPER

Michels, J., D. Venkatesh, C. Liu, S. Budhu, H. Zhong, M.M. George, D. Thach, Z.-K. Yao, O. Ouerfelli, H. Liu, B.R. Stockwell, L.F. Campesato, D. Zamarin, R. Zappasodi, J.D. Wolchok, and T. Merghoub. 2023. APR-246 increases tumor antigenicity independent of p53. *Life Science Alliance*. 7 (1): e202301999. https://doi.org/10.26508/lsa.202301999

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