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Machine Learning Discoveries of STEAP3-X Synergy in ETC-1922159 Treated Colorectal Cancer Cells

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Abstract: Six-transmembrane epithelial antigen of prostate 3 (STEAP3) is a metalloreductase that is capable of converting iron from an insoluble ferric (Fe^{3+}) to a soluble ferrous (Fe^{2+}) form. It has been found to be overexpressed in colorectal cancer. In colorectal cancer cells treated with ETC-1922159, it was found to be down-regulated. A recently developed search engine ranked combinations of STEAP3-X (X, a particular gene/protein) at 2^{nd} order level after drug administration. In this research work, I cover combinations of STEAP3 with cyclin dependent kinase inhibitor (CDKN), glutathione peroxidase (GPX), solute carrier family (SLC), methyltransferase N6 adenosine methyltransferase complex catalytic subunit (METTL), b-cell leukemia / lymphoma protein (BCL), interleukin (IL) and transferrin receptor protein (TFR) family.

Keywords: STEAP3; porcupine inhibitor ETC-1922159; sensitivity analysis; colorectal cancer

1. Introduction

1.1. Six-Transmembrane Epithelial Antigen of Prostate (STEAP)

Sendamarai et al. [1] discuss the role of STEAP3 as a metalloreductase. They state that erythroid precursor cells uptake iron (Fe^{3+}) by loading it to transferrin (TF) which then binds to the transferrin receptor (TFR) at the cell surface. This TF-TFR complex then enters the endosome. Upon endosomal acidification, iron is released from TF, reduced to Fe^{2+} by STEAP3, and transported across the endosomal membrane by a divalent metal iron transporter. Ohgami et al. [2] further characterize and demonstrate that STEAP2, STEAP3, and STEAP4 not only reduce iron but also copper. Zhou et al. [3] and Lv et al. [4] show that STEAP3 promotes colorectal cancer. In colorectal cancer cells treated with ETC-1922159, STEAP3 was found to be down regulated, along with other genes. I present here machine learning based discoveries of STEAP3-X combinations that might be working synergistically in colorectal cancer. Some of these combinations have already been tested in wet lab, however many others remain unexplored/untested. To address this, I use the following search engine, in the next section.

1.2. Combinatorial Search Problem and a Possible Solution

In a recently published work Sinha [5], a frame work of a search engine was developed which can rank combinations of factors (genes/proteins) in a signaling pathway. Readers are requested to go through the adaptation of the above mentioned work for gaining deeper insight into the working of the pipeline and its use of published data set generated after administration of ETC-1922159, Sinha [6]. The work uses SVM package by Joachims [7] in https://www.cs.cornell.edu/people/tj/svm_light/svm_rank.html. I use the adaptation to rank 2^{nd} order gene combinations.

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2. Results & Discussion

2.1. STEAP3 Related Synergies

2.1.1. STEAP3-CDKN Family

In colon cancer, Na et al. [8] STEAP3 overexpression upregulated the expression of CDKN1C. In colorectal cancer cells treated with ETC-1922159, some of the family members of CDKN were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of CDKN family members with STEAP3, that were down regulated.

Table 1 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 2 generated from analysis of the ranks in table 1. The table 1 shows rankings of CDKN family w.r.t STEAP3. CDKN2C - STEAP3 shows low ranking of 906 (laplace) and 118 (linear). CDKN3 - STEAP3 shows low ranking of 1369 (laplace) and 223 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment. CDKN2AIPNL did not show synergistic down regulation with STEAP3.

Table 1. 2^{nd} order interaction ranking between STEAP3 VS CDKN family members.

RANKING CDKN FAMILY VS STEAP3			
RANKING OF CDKN FAMILY W.R.T STEAP3			
	laplace	linear	rbf
CDKN2C - STEAP3	906	118	2200
CDKN3 - STEAP3	1369	223	2556
CDKN2AIPNL - STEAP3	2353	1642	1362

One can also interpret the results of the table 1 graphically, with the following influences - • CDKN family w.r.t STEAP3 with STEAP3 $->$ CDKN-2C/3.

Table 2. 2^{nd} order combinatorial hypotheses between STEAP3 and CDKN family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
CDKN family w.r.t STEAP3	
CDKN-2C/3	STEAP3

2.1.2. STEAP3-GPX family

In renal cell carcinoma, Ye et al. [9] show that in STEAP3 knockdown group, expression of othe ferroptosis-related protein GPX4 was decreased. Similarly, Han et al. [10] show that knockdown of STEAP3 decreased the expression of GPX4 in ovarian cancer cells. In colorectal cancer cells treated with ETC-1922159, some of the family members of GPX were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of GPX family members with STEAP3, that were down regulated.

Table 3 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 4 generated from analysis of the ranks in table 3. The table 3 shows rankings of

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GPX family w.r.t STEAP3. GPX1 - STEAP3 shows low ranking of 333 (linear) and 812 (rbf). GPX1P1 - STEAP3 shows low ranking of 1064 (linear) and 1610 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Table 3. 2^{nd} order interaction ranking between STEAP3 VS GPX family members.

RANKING GPX FAMILY VS STEAP3			
RANKING OF GPX FAMILY W.R.T STEAP3			
	laplace	linear	rbf
GPX1 - STEAP3	2124	333	812
GPX1P1 - STEAP3	2328	1064	1610

One can also interpret the results of the table 3 graphically, with the following influences - • GPX family w.r.t STEAP3 with STEAP3 $->$ GPX-1/1P1.

Table 4. 2^{nd} order combinatorial hypotheses between STEAP3 and GPX family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
GPX family w.r.t STEAP3	
GPX-1/1P1	STEAP3

2.1.3. STEAP3-SLC family

Han et al. [10] show that knockdown of STEAP3 decreased the expression of SLC7A11 in ovarian cancer cells. In colorectal cancer cells treated with ETC-1922159, some of the family members of SLC were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of SLC family members with STEAP3, that were down regulated.

Table 5 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 6 generated from analysis of the ranks in table 5. The table 5 shows rankings of SLC family w.r.t STEAP3. SLC19A3 - STEAP3 shows low ranking of 3 (laplace) and 58 (rbf). SLC25A19 - STEAP3 shows low ranking of 56 (laplace) and 600 (rbf). SLC39A10 - STEAP3 shows low ranking of 79 (laplace) and 292 (rbf). SLC12A8 - STEAP3 shows low ranking of 104 (laplace) and 846 (rbf). SLC25A35 - STEAP3 shows low ranking of 259 (laplace), 651 (linear) and 728 (rbf). SLC28A3 - STEAP3 shows low ranking of 272 (laplace), 1113 (linear) and 458 (rbf). SLC7A8 - STEAP3 shows low ranking of 368 (laplace), 559 (linear) and 887 (rbf). SLC19A1 - STEAP3 shows low ranking of 429 (laplace) and 1395 (linear). SLC25A26 - STEAP3 shows low ranking of 548 (laplace), 230 (linear) and 982 (rbf). SLC16A1.AS1 - STEAP3 shows low ranking of 690 (laplace), 1232 (linear) and 541 (rbf). SLC25A27 - STEAP3 shows low ranking of 1105 (laplace), 380 (linear) and 1569 (rbf). SLC35G1 - STEAP3 shows low ranking of 1108 (laplace) and 1302 (rbf). SLC39A8 - STEAP3 shows low ranking of 1175 (laplace) and 1564 (linear). SLC17A9 - STEAP3 shows low ranking of 1319 (laplace), 777 (linear) and 191 (rbf). SLC43A3 - STEAP3 shows low ranking of 1336 (laplace) and 341 (linear). SLC35E3 - STEAP3 shows low ranking of 922 (linear) and 690 (rbf). SLC12A2 - STEAP3 shows low ranking of 150 (linear) and

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1223 (rbf). SLC25A32 - STEAP3 shows low ranking of 1203 (linear) and 1426 (rbf). SLC38A5 - STEAP3 shows low ranking of 1151 (linear) and 1343 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

On the other hand, SLC4A7, SLC1A4, SLC18B1, SLC25A38, SLC28A2, SLC41A1, SLC25A15, SLC5A6, SLC35F2, SLC7A2, SLC43A1, SLC2A11, SLC25A14, SLC26A2, SLC25A40 and SLC6A6 do not show synergy with STEAP3 while synergistic down regulation.

Table 5. 2^{nd} order interaction ranking between STEAP3 VS SLC family members.

RANKING SLC FAMILY VS STEAP3							
	RANKING OF SLC FAMILY W.R.T STEAP3						
	laplace	linear	rbf		laplace	linear	rbf
SLC19A3 - STEAP3	3	2632	58	SLC25A19 - STEAP3	56	2618	600
SLC39A10 - STEAP3	79	1648	292	SLC12A8 - STEAP3	104	2463	846
SLC25A35 - STEAP3	259	651	728	SLC28A3 - STEAP3	272	1113	458
SLC7A8 - STEAP3	368	559	887	SLC4A7 - STEAP3	417	2258	2277
SLC19A1 - STEAP3	429	1395	2288	SLC25A26 - STEAP3	548	230	982
SLC1A4 - STEAP3	654	1931	1557	SLC16A1.AS1 - STEAP3	690	1232	541
SLC25A27 - STEAP3	1105	380	1569	SLC35G1 - STEAP3	1108	1654	1302
SLC39A8 - STEAP3	1175	1564	1803	SLC18B1 - STEAP3	1318	1670	1853
SLC17A9 - STEAP3	1319	777	191	SLC43A3 - STEAP3	1336	341	1777
SLC25A38 - STEAP3	1519	1768	1697	SLC28A2 - STEAP3	1573	2082	931
SLC35E3 - STEAP3	1589	922	690	SLC41A1 - STEAP3	1591	2516	1965
SLC25A15 - STEAP3	1623	1703	624	SLC5A6 - STEAP3	1671	1866	1668
SLC35F2 - STEAP3	1734	107	1842	SLC43A1 - STEAP3	1832	431	2423
SLC7A2 - STEAP3	1942	302	2648	SLC12A2 - STEAP3	1991	150	1223
SLC25A32 - STEAP3	2063	1203	1426	SLC2A11 - STEAP3	2101	1991	1404
SLC25A14 - STEAP3	2120	308	2254	SLC26A2 - STEAP3	2240	1658	964
SLC25A40 - STEAP3	2269	1371	2206	SLC6A6 - STEAP3	2576	1519	2482
SLC38A5 - STEAP3	2682	1151	1343				

One can also interpret the results of the table 5 graphically, with the following influences - • SLC family w.r.t STEAP3 with STEAP3 $->$ SLC-19A3 / 25A19 / 39A10 / 12A8 / 25A35 / 28A3 / 7A8 / 19A1 / 25A26 / 16A1.AS1 / 25A27 / 35G1 / 39A8 / 17A9 / 43A3 / 35E3 / 12A2 / 25A32 / 38A5.

Table 6. 2^{nd} order combinatorial hypotheses between STEAP3 and SLC family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
SLC family w.r.t STEAP3	
SLC-19A3/25A19/39A10/12A8/25A35/28A3/7A8/19A1	STEAP3
SLC-25A26/16A1.AS1/25A27/35G1/39A8/17A9/43A3	STEAP3
SLC-35E3/12A2/25A32/38A5	STEAP3

2.1.4. STEAP3-METTL family

In colorectal cancer, Zhou et al. [3] determined the related regulators for STEAP3 m^6A modification, by knocking down m^6A writers (METTL3, METTL14) and m^6A readers (YTHDF1, YTHDF2). Their experiments shows that the protein level and mRNA level of STEAP3 were decreased by METTL14 and YTHDF2. In colorectal cancer cells treated with ETC-1922159, some of the family members of METTL were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of METTL family members with STEAP3, that were down regulated.

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Table 7 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 8 generated from analysis of the ranks in table 7. The table 7 shows rankings of METTL family w.r.t STEAP3. METTL3 - STEAP3 shows low ranking of 156 (laplace) and 326 (rbf). METTL16 - STEAP3 shows low ranking of 799 (laplace) and 654 (rbf). METTL12 - STEAP3 shows low ranking of 884 (laplace), 1147 (linear) and 687 (rbf). METTL21B - STEAP3 shows low ranking of 1228 (laplace) and 995 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment. However, METTL1, METTL8, METTL13, METTL5, METTL21A, METTL17 and METTL2B did not show any down regulation synergy with STEAP3.

Table 7. 2^{nd} order interaction ranking between STEAP3 VS METTL family members.

RANKING METTL FAMILY VS STEAP3			
RANKING OF METTL FAMILY W.R.T STEAP3			
	laplace	linear	rbf
METTL3 - STEAP3	156	1958	326
METTL16 - STEAP3	799	2196	654
METTL12 - STEAP3	884	1147	687
METTL21B - STEAP3	1228	2012	995
METTL1 - STEAP3	1579	1553	689
METTL8 - STEAP3	1659	2592	1638
METTL13 - STEAP3	1721	2335	1346
METTL5 - STEAP3	1960	1544	2485
METTL21A - STEAP3	2154	1937	1446
METTL17 - STEAP3	2239	1126	2370
METTL2B - STEAP3	2689	74	2242

One can also interpret the results of the table 7 graphically, with the following influences - • METTL family w.r.t STEAP3 with STEAP3 $->$ METTL-3/16/12/21B.

Table 8. 2^{nd} order combinatorial hypotheses between STEAP3 and METTL family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
METTL family w.r.t STEAP3	
METTL-3/16/12/21B	STEAP3

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2.1.5. STEAP3-BCL family

In hepatocellular carcinoma, citetWang:2021steap3 STEAP3 promotes cancer cell proliferation. They found that anti-apoptotic protein BCL2 was substantially transcriptionally upregulated by STEAP3. In colorectal cancer cells treated with ETC-1922159, some of the family members of BCL were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of BCL family members with STEAP3, that were down regulated.

Table 9 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 10 generated from analysis of the ranks in table 9. The table 9 shows rankings of BCL family w.r.t STEAP3. BCL6B - STEAP3 shows low ranking of 65 (laplace) and 100 (rbf). BCL11A - STEAP3 shows low ranking of 854 (laplace) and 1322 (rbf). BCL11B - STEAP3 shows low ranking of 1026 (laplace) and 691 (rbf). BCL2L12 - STEAP3 shows low ranking of 1035 (laplace) and 1292 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment. However, BCL9 and BCL7A did not show any down regulation synergy with STEAP3.

Table 9. 2^{nd} order interaction ranking between STEAP3 VS BCL family members.

RANKING BCL FAMILY VS STEAP3			
RANKING OF BCL FAMILY W.R.T STEAP3			
	laplace	linear	rbf
BCL6B - STEAP3	65	2708	100
BCL11A - STEAP3	854	1793	1322
BCL11B - STEAP3	1026	2624	691
BCL2L12 - STEAP3	1035	1292	2235
BCL9 - STEAP3	2265	558	1963
BCL7A - STEAP3	2597	739	2309

One can also interpret the results of the table 9 graphically, with the following influences - • BCL family w.r.t STEAP3 with STEAP3 $-$ > BCL-6B/11A/11B/2L12.

Table 10. 2^{nd} order combinatorial hypotheses between STEAP3 and BCL family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
BCL family w.r.t STEAP3	
BCL-6B/11A/11B/2L12	STEAP3

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2.1.6. STEAP3-IL family

In hepatocellular carcinoma, Wang et al. [11] STEAP3 promotes cancer cell proliferation. They found that inflammatory factors like IL-8 and IL-18 were substantially transcriptionally upregulated by STEAP3. In colorectal cancer cells treated with ETC-1922159, some of the family members of IL were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of IL family members with STEAP3, that were down regulated.

Table 11 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 12 generated from analysis of the ranks in table 11. The table 11 shows rankings of IL family w.r.t STEAP3. ILF3 - STEAP3 shows low ranking of 121 (laplace) and 926 (rbf). IL17RB - STEAP3 shows low ranking of 208 (laplace) and 404 (rbf). IL17D - STEAP3 shows low ranking of 596 (laplace) and 705 (linear). IL33 - STEAP3 shows low ranking of 1070 (laplace) and 57 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment. However, IL1RL2, ILF2 and IL17RD did not show any down regulation synergy with STEAP3.

Table 11. 2^{nd} order interaction ranking between STEAP3 VS IL family members.

RANKING IL FAMILY VS STEAP3			
RANKING OF IL FAMILY W.R.T STEAP3			
	laplace	linear	rbf
ILF3 - STEAP3	121	2314	926
IL17RB - STEAP3	208	2462	404
IL17D - STEAP3	596	705	2273
IL1RL2 - STEAP3	835	2234	1733
IL33 - STEAP3	1070	57	2098
ILF2 - STEAP3	1986	1029	2474
IL17RD - STEAP3	2352	589	2233

One can also interpret the results of the table 11 graphically, with the following influences - • IL family w.r.t STEAP3 with STEAP3 $-$ > IL-F3/17RB/17D/33.

Table 12. 2^{nd} order combinatorial hypotheses between STEAP3 and IL family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
IL family w.r.t STEAP3	
IL-F3/17RB/17D/33	STEAP3

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2.1.7. STEAP3-TFR Family

Ohgami et al. [2], show that the expression of STEAP2 and STEAP4 in erythropoietic tissues, their partial colocalization with TF and TFR1, and the demonstration that they have ferrireductase activity in vitro, indicate that STEAP2 and STEAP4 are reasonable candidates for redundant ferrireductases in the erythroid TF-cycle endosome. In colorectal cancer cells treated with ETC-1922159, some of the family members of TFR were down regulated, along with STEAP3. Individual recordings of these down regulations have been documented. I was able to rank 2^{nd} order combination of TFR family members with STEAP3, that were down regulated.

Table 13 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in table 14 generated from analysis of the ranks in table 13. The table 13 shows rankings of TFR family w.r.t STEAP3. TFR2 - STEAP3 shows low ranking of 1063 (laplace) and 1169 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment. However, TFRC did not show any down regulation synergy with STEAP3.

Table 13. 2^{nd} order interaction ranking between STEAP3 VS TFR family members.

RANKING TFR FAMILY VS STEAP3			
RANKING OF TFR FAMILY W.R.T STEAP3			
	laplace	linear	rbf
TFR2 - STEAP3	1063	2487	1169
TFRC - STEAP3	1946	663	2255

One can also interpret the results of the table 13 graphically, with the following influences - • TFR family w.r.t STEAP3 with STEAP3 $-$ > TFR-2.

Table 14. 2^{nd} order combinatorial hypotheses between STEAP3 and TFR family members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
TFR family w.r.t STEAP3	
TFR-2	STEAP3

3. Conclusion

Presented here are a range of multiple synergistic STEAP3 2^{nd} order combinations that were ranked via a machine learning based search engine. Via majority voting across the ranking methods, it was possible to find plausible unexplored synergistic combinations of STEAP3-X that might be prevalent in CRC cells after treatment with ETC-1922159 drug.

Author Contributions: Concept, design, in silico implementation - SS. Analysis and interpretation of results - SS. Manuscript writing - SS. Manuscript revision - SS. Approval of manuscript - SS.

Data Availability Statement: Data used in this research work was released in a publication in Madan et al. [12]. The ETC-1922159 was released in Singapore in July 2015 under the flagship of the Agency for Science, Technology and Research (A*STAR) and Duke-National University of Singapore Graduate Medical School (Duke-NUS).

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Conflicts of Interest: There are no conflicts to declare.

References

1. Sendamarai, A.K.; Ohgami, R.S.; Fleming, M.D.; Lawrence, C.M. Structure of the membrane proximal oxidoreductase domain of human Steap3, the dominant ferrireductase of the erythroid transferrin cycle. *Proceedings of the National Academy of Sciences* **2008**, *105*, 7410–7415.
2. Ohgami, R.S.; Campagna, D.R.; McDonald, A.; Fleming, M.D. The Steap proteins are metalloreductases. *Blood* **2006**, *108*, 1388–1394.
3. Zhou, L.; Jiang, J.; Huang, Z.; Jin, P.; Peng, L.; Luo, M.; Zhang, Z.; Chen, Y.; Xie, N.; Gao, W.; et al. Hypoxia-induced lncRNA STEAP3-AS1 activates Wnt/β-catenin signaling to promote colorectal cancer progression by preventing m6A-mediated degradation of STEAP3 mRNA. *Molecular cancer* **2022**, *21*, 168.
4. Lv, J.; Liu, X.; Sun, Z.; Gao, J.; Yu, X.; Zhang, M.; Zhang, Z.; Ren, S.; Zuo, Y. STEAP3 promotes colon cancer cell proliferation and migration via regulating histone acetylation. *Human Genetics* **2024**, *143*, 343–355.
5. Sinha, S. Machine learning ranking of plausible (un) explored synergistic gene combinations using sensitivity indices of time series measurements of Wnt signaling pathway. *Integrative Biology* **2024**, *16*, zyae020.
6. Sinha, S. Sensitivity analysis based ranking reveals unknown biological hypotheses for down regulated genes in time buffer during administration of PORCN-WNT inhibitor ETC-1922159 in CRC. *bioRxiv* **2017**, p. 180927.
7. Joachims, T. Training linear SVMs in linear time. In Proceedings of the Proceedings of the 12th ACM SIGKDD international conference on Knowledge discovery and data mining. ACM, 2006, pp. 217–226.
8. Na, H.; Li, X.; Zhang, X.; Xu, Y.; Sun, Y.; Cui, J.; Chen, Z.; Shi, X.; Ren, S.; Zuo, Y. lncRNA STEAP3-AS1 modulates cell cycle progression via affecting CDKN1C expression through STEAP3 in colon cancer. *Molecular Therapy-Nucleic Acids* **2020**, *21*, 480–491.
9. Ye, C.L.; Du, Y.; Yu, X.; Chen, Z.Y.; Wang, L.; Zheng, Y.F.; Liu, X.H. STEAP3 affects ferroptosis and progression of renal cell carcinoma through the p53/xCT pathway. *Technology in Cancer Research & Treatment* **2022**, *21*, 15330338221078728.
10. Han, Y.; Fu, L.; Kong, Y.; Jiang, C.; Huang, L.; Zhang, H. STEAP3 affects ovarian cancer progression by regulating ferroptosis through the p53/SLC7A11 pathway. *Mediators of Inflammation* **2024**, *2024*, 4048527.
11. Wang, L.L.; Luo, J.; He, Z.H.; Liu, Y.Q.; Li, H.G.; Xie, D.; Cai, M.Y. STEAP3 promotes cancer cell proliferation by facilitating nuclear trafficking of EGFR to enhance RAC1-ERK-STAT3 signaling in hepatocellular carcinoma. *Cell Death & Disease* **2021**, *12*, 1052.
12. Madan, B.; Ke, Z.; Harmston, N.; Ho, S.Y.; Frois, A.; Alam, J.; Jeyaraj, D.A.; Pendharkar, V.; Ghosh, K.; Virshup, I.H.; et al. Wnt addiction of genetically defined cancers reversed by PORCN inhibition. *Oncogene* **2016**, *35*, 2197.