Article

Not peer-reviewed version

Machine Learning Discoveries of RHNO1-X Synergy in ETC-1922159 Treated Colorectal Cancer Cells

Shriprakash Sinha *

Posted Date: 13 January 2025

doi: 10.20944/preprints202501.0910.v1

Keywords: RHNO1; porcupine inhibitor ETC-1922159; sensitivity analysis; machine learning; colorectal cancer

 doi:10.20944/preprints202501.0910.v1

Article

Machine Learning Discoveries of RHNO1-X Synergy in ETC-1922159 Treated Colorectal Cancer Cells

Shriprakash Sinha

Independent Researcher; Orcid ID: orcid.org/0000-0001-7027-5788
104-Madhurisha Heights Phase 1, Risali, Bhilai-490006, India; sinha.shriprakash@yandex.com

* ML dicoveries of RHNO1-X synergy in ETC-1922159 treated CRC cells

[1] Aspects of unpublished work were presented in a poster session at the first Wnt Gordon Research Conference, from 6-11 August 2017, held in Stowe, VT 05672, USA

Abstract: In response to DNA damage and replication stress, RHINO RAD9-HUS1-RAD1 interacting nuclear orphan (RHNO1), interacts with RAD9-HUS1-RAD1 (9-1-1) clamp and TOPBP1, to activate ATR signaling pathway. Recently, it has been found to be implicated in cancer as it is often overexpressed. In colorectal cancer (CRC) cells treated with ETC-1922159, RHNO1 was found to be down regulated along with other genes. A recently developed search engine ranked combinations of RHNO1-X (X, a particular gene/protein) at 2^{nd} order level after drug administration. Some of these combinations have been tested in wet lab, however many have been pointed out by the search engine that are yet to be explored/tested. These rankings reveal which RHNO1-X combinations might be working synergistically in CRC. In this research work, I cover combinations of RHNO1 with possible members of DNA topoisomerase (TOP), nei like DNA glycosylase (NEIL), flap structure-specific endonuclease 1 (FEN1), tumor protein p53 (TP53), ATR serine/threonine kinase (ATR), cell division cycle (CDC), forkhead box (FOX) and bone morphogenetic protein (BMP) family.

Keywords: RHNO1; porcupine inhibitor ETC-1922159; sensitivity analysis; machine learning; colorectal cancer

1. Introduction

1.1. RHNO1

In response to DNA damage and replication stress, the DNA damage response (DDR) a protein kinase cascade is intiated. This initiation leads to cell cycle arrest. RHNO1, interacts with RAD9-HUS1-RAD1 (9-1-1) clamp and TOPBP1, which is then recruited to the sites of DNA damage to activate ATR signaling pathway (Cotta-Ramusino et al. [1]). RHNO1, previously known as chromosome 12 open reading frame 32 (C12orf32), was found to be overexpressed in breast cancer cells, as discovered by Kim et al. [2]. They showed that depletion of C12orf32 expression suppressed the growth of breast cancer cell lines. Lindsey-Boltz et al. [3] show that RHNO1 directly binds to TOPBP1 and forms a stable stoichiometric complex with 9-1-1, which further mediates ATR DNA damage checkpoint signaling in mammalian cells.

In hepatocellular carcinoma (HCC), Du et al. [4] found that RHNO1 protein levels were increased in most cells and knockdown of RHNO1 inhibited the proliferation and triggered cell mitochondrial apoptosis by inactivating the PI3K/AKT pathway. Recently, in their review, Jirapongwattana et al. [5] discuss the structure and role of RHNO1, in DNA replication stress, DNA repair, and cancer. In colorectal cancer (CRC) cells treated with ETC-1922159, RHNO1 was found to be down regulated along with other genes. Some combinations of RHNO1 have been confirmed in wet lab, however, many of the combinations have not been explored/tested or are known. To reveal these combinations, I use a modification of a recently published machine learning based search engine, details of which are given in the next section.

 doi:10.20944/preprints202501.0910.v1

1.2. Combinatorial Search Problem and a Possible Solution

In a recently published work Sinha [6], 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 [7]. The work uses SVM package by Joachims [8] in https://www.cs.cornell.edu/people/tj/svm_light/svm_rank.html. I use the adaptation to rank 2^{nd} order gene combinations.

2. Results & Discussion

2.1. RHNO1 Related Synergies

2.1.1. RHNO1 - TOP

From the references in introduction section, it is known that RHNO1 binds with TOPBP1, along with 9-1-1 clamp to activate ATR signaling pathway, in response to DNA damage and replication stress. A further advancement by Day et al. [9] has lead to the indentification of TOPBP1-BRCT-1/2 binding site in RHNO1. In colorectal cancer cells treated with ETC-1922159, TOP family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these TOP members along with RHNO1.

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 TOP members w.r.t RHNO1. TOPBP1 - RHNO1 shows low ranking of 1201 (laplace), 136 (linear) and 357 (rbf). TOP1MT - RHNO1 shows low ranking of 325 (laplace), 1254 (linear) and 889 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Further, TOPA2 and TOP2B showed high ranking with RHNO1, thus indicating that they might not be working synergistically with RHNO1, before the drug treatment.

Table 1. 2^{nd} order interaction ranking between RHNO1 VS TOP members.

RANKING TOP FAMILY VS RHNO1			
RANKING OF TOP FAMILY W.R.T RHNO1			
	laplace	linear	rbf
TOPBP1 - RHNO1	1201	136	357
TOP2B - RHNO1	1806	1649	942
TOP2A - RHNO1	190	1779	2080
TOP1MT - RHNO1	325	1254	889

One can also interpret the results of the Table 1 graphically, with the following influences - • TOP members w.r.t RHNO1 with RHNO1 − > TOP-BP1/1MT.

Table 2. 2^{nd} order combinatorial hypotheses between RHNO1 and TOP members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
TOP members w.r.t RHNO1	
TOP-BP1/1MT	RHNO1

2.1.2. RHNO1 - NEIL

McDonald et al. [10] study the protein-protein interactions of NEIL1 glycosylase and the checkpoint protein 9-1-1 complex and discovered interactions between the two. Since RHNO1 also interacts with 9-1-1 complex, but it is not known that there is an interaction (direct/indirect) between RHNO1 and NEIL family, it would be great to see what the search engine points to regarding RHNO1 and NEIL family members. In colorectal cancer cells treated with ETC-1922159, NEIL family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these NEIL members along with RHNO1.

 doi:10.20944/preprints202501.0910.v1

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 NEIL members w.r.t RHNO1. NEIL1 - RHNO1 shows low ranking of 592 (laplace) and 851 (rbf). NEIL2 - RHNO1 shows low ranking of 1351 (laplace) and 68 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Further, NEIL3 showed high ranking with RHNO1, thus indicating that they might not be working synergistically with RHNO1, before the drug treatment.

Table 3. 2^{nd} order interaction ranking between RHNO1 VS NEIL members.

RANKING NEIL FAMILY VS RHNO1			
RANKING OF NEIL FAMILY W.R.T RHNO1			
	laplace	linear	rbf
NEIL1 - RHNO1	592	851	2143
NEIL2 - RHNO1	1351	68	2293
NEIL3 - RHNO1	2672	241	1935

One can also interpret the results of the Table 3 graphically, with the following influences - • NEIL members w.r.t RHNO1 with RHNO1 − > NEIL-1/2.

Table 4. 2^{nd} order combinatorial hypotheses between RHNO1 and NEIL members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
NEIL members w.r.t RHNO1	
NEIL-1/2	RHNO1

2.1.3. RHNO1 - FEN1

Similar to the case of NEIL1 above, Shi et al. [11] observe in their previous study that in response to DNA damage, FEN1 interacts with the RAD9-HUS1-RAD1 complex instead of PCNA to engage in DNA repair activities, and undergoes SUMOylation by SUMO1. Further, FEN1 succinylation regulates DNA replication and repair, thus maintaining genome stability. Since FEN1 also interacts with 9-1-1 complex, but it is not known that there is an interaction (direct/indirect) between RHNO1 and FEN1, it would be great to see what the search engine points to regarding RHNO1 and FEN1. In colorectal cancer cells treated with ETC-1922159, FEN1 and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of FEN1 along with RHNO1.

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 FEN1 members w.r.t RHNO1. FEN1 - RHNO1 shows low ranking of 212 (laplace) and 1354 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Table 5. 2^{nd} order interaction ranking between RHNO1 VS FEN1 members.

RANKING FEN1 FAMILY VS RHNO1			
RANKING OF FEN1 FAMILY W.R.T RHNO1			
	laplace	linear	rbf
FEN1 - RHNO1	212	1354	2568

One can also interpret the results of the table 5 graphically, with the following influences - • FEN1 members w.r.t RHNO1 with RHNO1 − > FEN1.

 doi:10.20944/preprints202501.0910.v1

Table 6. 2^{nd} order combinatorial hypotheses between RHNO1 and FEN1 members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
FEN1 members w.r.t RHNO1	
FEN1	RHNO1

2.1.4. RHNO1 - TP53

Bigot et al. [12] show that the DNA damage checkpoint regulating S-phase entry is controlled by a phosphorylation-dependent interaction of 53BP1 (or TP53BP1) and TOPBP1, through BRCT domains. Also, TOPBP1 interaction with 53BP1 is structurally complimentary to its interaction with RAD9-HUS1-RAD1. Since RHNO1 also interacts with 9-1-1 complex, but it is not known that there is an interaction (direct/indirect) between RHNO1 and TP53 family, it would be great to see what the search engine points to regarding RHNO1 and TP53 family members. In colorectal cancer cells treated with ETC-1922159, TP53 family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these TP53 members along with RHNO1.

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 TP53 members w.r.t RHNO1. TP53BP1 - RHNO1 shows low ranking of 776 (laplace), 1507 (linear) and 229 (rbf). TP53 - RHNO1 shows low ranking of 1338 (laplace) and 1540 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Table 7. 2^{nd} order interaction ranking between RHNO1 VS TP53 members.

RANKING TP53 FAMILY VS RHNO1			
RANKING OF TP53 FAMILY W.R.T RHNO1			
	laplace	linear	rbf
TP53BP1 - RHNO1	776	1507	229
TP53 - RHNO1	1338	1540	1635

One can also interpret the results of the Table 7 graphically, with the following influences - • TP53 members w.r.t RHNO1 with RHNO1 − > TP-53/53BP1.

Table 8. 2^{nd} order combinatorial hypotheses between RHNO1 and TP53 members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
TP53 members w.r.t RHNO1	
TP-53/53BP1	RHNO1

2.1.5. RHNO1 - ATR

Du et al. [4] indicate through references that RHNO1 was recognized as a DNA damage response (DDR) regulator through interaction with 9-1-1 clamp and TOPBP1, thus activating ATR and its downstream CHK1 pathway, to respond to replication stress. In colorectal cancer cells treated with ETC-1922159, ATR family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these ATR members along with RHNO1.

The Table 9 shows rankings of ATR members w.r.t RHNO1. Interestingly, both ATRIP and ATR showed high ranking with RHNO1, thus indicating that they might not be working synergistically with RHNO1, before the drug treatment.

 doi:10.20944/preprints202501.0910.v1

Table 9. 2^{nd} order interaction ranking between RHNO1 VS ATR members.

RANKING ATR FAMILY VS RHNO1			
RANKING OF ATR FAMILY W.R.T RHNO1			
	laplace	linear	rbf
ATR-IP - RHNO1	2092	161	2274
ATR - RHNO1	2641	2711	2071

2.1.6. RHNO1 - CDC

Sorensen et al. [13] show that during the S phase, the regulation of the CHK1-CDC25A pathway depends on ATR, Claspin, RAD9, and HUS1. We also know from previously mentioned discussion that ATR is regulated by RHNO1. Thus it might be suspected that there exists a synergy between RHNO1 and CDC family members. In colorectal cancer cells treated with ETC-1922159, CDC family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these CDC members along with RHNO1.

Table 10 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in Table 11 generated from analysis of the ranks in Table 10. The Table 10 shows rankings of CDC members w.r.t RHNO1. CDCA5 - RHNO1 shows low ranking of 100 (laplace) and 1106 (rbf). CDCA7 - RHNO1 shows low ranking of 119 (laplace) and 1431 (rbf). CDC45 - RHNO1 shows low ranking of 141 (laplace) and 47 (rbf). CDC25C - RHNO1 shows low ranking of 167 (laplace) and 1134 (rbf). CDCA7L - RHNO1 shows low ranking of 221 (laplace) and 275 (rbf). CDC25A - RHNO1 shows low ranking of 396 (laplace), 995 (linear) and 841 (rbf). CDC7 - RHNO1 shows low ranking of 426 (laplace), 1385 (linear) and 1152 (rbf). CDC6 - RHNO1 shows low ranking of 620 (laplace) and 1115 (linear). CDCA3 - RHNO1 shows low ranking of 679 (laplace) and 264 (rbf). CDCA2 - RHNO1 shows low ranking of 796 (laplace) and 671 (rbf). CDC123 - RHNO1 shows low ranking of 1097 (laplace) and 712 (rbf). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Further, CDC20, CDC23, CDCA4 and CDCA8 showed high ranking with RHNO1, thus indicating that they might not be working synergistically with RHNO1, before the drug treatment.

Table 10. 2^{nd} order interaction ranking between RHNO1 VS CDC members.

RANKING CDC FAMILY VS RHNO1			
RANKING OF CDC FAMILY W.R.T RHNO1			
	laplace	linear	rbf
CDC20 - RHNO1	75	2116	1779
CDCA5 - RHNO1	100	1845	1106
CDCA7 - RHNO1	119	2714	1431
CDC45 - RHNO1	141	1622	47
CDC25C - RHNO1	167	1865	1134
CDCA7L - RHNO1	221	2468	275
CDC25A - RHNO1	396	995	841
CDC7 - RHNO1	426	1385	1152
CDC6 - RHNO1	620	1115	2015
CDCA3 - RHNO1	679	2082	264
CDCA2 - RHNO1	796	1770	671
CDC123 - RHNO1	1097	1829	712
CDC23 - RHNO1	1599	1630	1262
CDCA4 - RHNO1	1674	1723	2309
CDCA8 - RHNO1	2002	2529	3

One can also interpret the results of the Table 10 graphically, with the following influences - • CDC members w.r.t RHNO1 with RHNO1 – > CDC-A5/A7/45/25C/A7L/25A/7/6/A3/A2/123.

 doi:10.20944/preprints202501.0910.v1

Table 11. 2^{nd} order combinatorial hypotheses between RHNO1 and CDC members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
CDC members w.r.t RHNO1	
CDC-A5/A7/45/25C/A7L/25A/7/6/A3/A2/123	RHNO1

2.1.7. RHNO1 - FOX

In high-grade serous carcinoma, Barger et al. [14] demonstrate that FOXM1 and RHNO1 are head-to-head (i.e., bidirectional) genes regulated by a bidirectional promoter named F/R-BDP. Thus, there is a synergy between FOXM1 and RHNO1. It might be suspected that there exists a synergy between RHNO1 and other FOX family members. In colorectal cancer cells treated with ETC-1922159, FOX family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these FOX members along with RHNO1.

Table 12 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in Table 13 generated from analysis of the ranks in Table 12. The Table 12 shows rankings of FOX members w.r.t RHNO1. FOXM1 - RHNO1 shows low ranking of 377 (laplace) and 1521 (rbf). FOXD2-AS1 - RHNO1 shows low ranking of 1090 (laplace) and 156 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

Further, FOXA2 and FOXJ1 showed high ranking with RHNO1, thus indicating that they might not be working synergistically with RHNO1, before the drug treatment.

Table 12. 2^{nd} order interaction ranking between RHNO1 VS FOX members.

RANKING FOX FAMILY VS RHNO1			
RANKING OF FOX FAMILY W.R.T RHNO1			
	laplace	linear	rbf
FOXM1 - RHNO1	377	2014	1521
FOXD2-AS1 - RHNO1	1090	156	2451
FOXA2 - RHNO1	2221	2684	1390
FOXJ1 - RHNO1	2555	1760	1502

One can also interpret the results of the Table 12 graphically, with the following influences - • FOX members w.r.t RHNO1 with RHNO1 – > FOX-M1/D2-AS1.

Table 13. 2^{nd} order combinatorial hypotheses between RHNO1 and FOX members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
FOX members w.r.t RHNO1	
FOX-M1/D2-AS1	RHNO1

2.1.8. RHNO1 - BMP

Xiong et al. [15] showed that lncRNA RHNO1/miR-6979-5p/BMP2 axis is a regulatory mechanism controlling osteoblast differentiation. In colorectal cancer cells treated with ETC-1922159, BMP family members and RHNO1, were found to be down regulated and their regulation was recorded independently. I was able to rank 2^{nd} order combination of these BMP members along with RHNO1.

Table 14 shows rankings of these combinations. Followed by this is the unexplored combinatorial hypotheses in Table 15 generated from analysis of the ranks in Table 14. The Table 14 shows rankings of BMP members w.r.t RHNO1. BMP7 - RHNO1 shows low ranking of 1179 (laplace) and 179 (linear). These rankings point to the synergy existing between the two components, which have been down regulated after the drug treatment.

 doi:10.20944/preprints202501.0910.v1

Table 14. 2^{nd} order interaction ranking between RHNO1 VS BMP members.

RANKING BMP FAMILY VS RHNO1			
RANKING OF BMP FAMILY W.R.T RHNO1			
	laplace	linear	rbf
BMP7 - RHNO1	1179	179	1814

One can also interpret the results of the Table 14 graphically, with the following influences - • BMP members w.r.t RHNO1 with RHNO1 − > BMP-7.

Table 15. 2^{nd} order combinatorial hypotheses between RHNO1 and BMP members.

UNEXPLORED COMBINATORIAL HYPOTHESES	
BMP members w.r.t RHNO1	
BMP-7	RHNO1

3. Conclusion

Presented here are a range of multiple synergistic RHNO1 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 RHNO1-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. [16].

Acknowledgments: Special thanks to Mrs. Rita Sinha and Mr. Prabhat Sinha for supporting the author financially, without which this work could not have been made possible.

Conflicts of Interest: There are no conflicts to declare.

References

1. C. Cotta-Ramusino, E. R. McDonald III, K. Hurov, M. E. Sowa, J. W. Harper, S. J. Elledge, A dna damage response screen identifies rhino, a 9-1-1 and topbp1 interacting protein required for atr signaling, Science 332 (2011) 1313–1317.
2. J.-W. Kim, C. Fukukawa, K. Ueda, T. Nishidate, T. Katagiri, Y. Nakamura, Involvement of c12orf32 overexpression in breast carcinogenesis, International journal of oncology 37 (2010) 861–867.
3. L. A. Lindsey-Boltz, M. G. Kemp, C. Capp, A. Sancar, Rhino forms a stoichiometric complex with the 9-1-1 checkpoint clamp and mediates atr-chk1 signaling, Cell Cycle 14 (2015) 99–108.
4. D. Du, S. Wang, T. Li, Z. Liu, M. Yang, L. Sun, S. Yuan, Rhno1 disruption inhibits cell proliferation and induces mitochondrial apoptosis via pi3k/akt pathway in hepatocellular carcinoma, Biochemical and Biophysical Research Communications 673 (2023) 96–105.
5. N. Jirapongwattana, S. F. Bunting, D. R. Ronning, G. Ghosal, A. R. Karpf, Rhno1: at the crossroads of dna replication stress, dna repair, and cancer, Oncogene 43 (2024) 2613–2620.
6. S. Sinha, Machine learning ranking of plausible (un) explored synergistic gene combinations using sensitivity indices of time series measurements of wnt signaling pathway, Integrative Biology 16 (2024) zyae020.
7. S. Sinha, 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) 180927.
8. T. Joachims, Training linear svms in linear time, in: Proceedings of the 12th ACM SIGKDD international conference on Knowledge discovery and data mining, ACM, 2006, pp. 217–226.
9. M. Day, M. Rappas, K. Ptasinska, D. Boos, A. W. Oliver, L. H. Pearl, Brct domains of the dna damage checkpoint proteins topbp1/rad4 display distinct specificities for phosphopeptide ligands, Elife 7 (2018) e39979.
10. D. T. McDonald, P. S. Wang, J. Moitoza Johnson, M.-S. Tsai, Using affinity pulldown assays to study protein–protein interactions of human neil1 glycosylase and the checkpoint protein rad9–rad1–hus1 (9-1-1) complex, in: Base Excision Repair Pathway: Methods and Protocols, Springer, 2023, pp. 199–207.

 doi:10.20944/preprints202501.0910.v1

11. R. Shi, Y. Wang, Y. Gao, X. Xu, S. Mao, Y. Xiao, S. Song, L. Wang, B. Tian, Y. Zhao, et al., Succinylation at a key residue of fen1 is involved in the dna damage response to maintain genome stability, American Journal of Physiology-Cell Physiology 319 (2020) C657–C666.
12. N. Bigot, M. Day, R. A. Baldock, F. Z. Watts, A. W. Oliver, L. H. Pearl, Phosphorylation-mediated interactions with topbp1 couple 53bp1 and 9-1-1 to control the g1 dna damage checkpoint, Elife 8 (2019) e44353.
13. C. S. Sorensen, R. G. Syljuasen, J. Lukas, J. Bartek, Atr, claspin and the rad9-rad1-hus1 complex regulate chk1 and cdc25a in the absence of dna damage, Cell cycle 3 (2004) 939–943.
14. C. J. Barger, L. Chee, M. Albahrani, C. Munoz-Trujillo, L. Boghean, C. Branick, K. Odunsi, R. Drapkin, L. Zou, A. R. Karpf, Co-regulation and function of foxm1/rhno1 bidirectional genes in cancer, Elife 10 (2021) e55070.
15. Y. Xiong, L. Chen, C. Yan, Y. Endo, B. Mi, G. Liu, The lncrna rhno1/mir-6979-5p/bmp2 axis modulates osteoblast differentiation, International Journal of Biological Sciences 16 (2020) 1604.
16. B. Madan, Z. Ke, N. Harmston, S. Y. Ho, A. Frois, J. Alam, D. A. Jeyaraj, V. Pendharkar, K. Ghosh, I. H. Virshup, et al., Wnt addiction of genetically defined cancers reversed by porcn inhibition, Oncogene 35 (2016) 2197.