**New Result:**

**The hypermethylation status of GALR1 and NTSR1 are validatd in our 6 NSCLC tissues compared with its adjacent tissues (Pvalue,0.011,0.013 respectively) . The methylation detection ratio of GALR1 is equal to the above data.**

**Gene function of four genes from data-analysis**

**GALR1,** galanin receptor subtype 2 suppresses cell proliferation in several cancers such as head and neck[[1](#_ENREF_1), [2](#_ENREF_2)],oral squamous cell carcinoma[[3](#_ENREF_3)]. And its inactivation can be caused by promoter hypermethyaltion[[1](#_ENREF_1)].

**SLC5A8,** a tumor suppressor gene,is usally suppressed in cancers[[4-6](#_ENREF_4)],Functional identification of SLC5A8, a tumor suppressor down-regulated in colon cancer, as a Na(+)-coupled transporter for short-chain fatty acids[[6](#_ENREF_6)]. Aberrant methylation and histone deacetylation associated with silencing of SLC5A8 in gastric cancer[[5](#_ENREF_5)]. Protein expressions and genetic variations of SLC5A8 in prostate cancer risk and aggressiveness[[7](#_ENREF_7)].

**Neurotensin receptor-1 (NTSR-1)** is a G-protein coupled receptor (GPCR) that has been recently identified as a mediator of cancer progression[[8](#_ENREF_8)].Neurotensin receptor 1 determines the outcome of non-small cell lung cancer[[9](#_ENREF_9)]. Inhibition of neurotensin receptor 1 selectively sensitizes prostate cancer to ionizing radiation[[10](#_ENREF_10)].The neurotensin receptor-1 promotes tumor development in a sporadic but not an inflammation-associated mouse model of colon cancer[[11](#_ENREF_11)]. The potential use of the neurotensin high affinity receptor 1 as a biomarker for cancer progression and as a component of personalized medicine in selective cancers[[12](#_ENREF_12)].

**AGTR1,** angiotensin II receptor type 1, is associated with cell proliferation[[13](#_ENREF_13)] and the cancer classfication in breast cancer[[14](#_ENREF_14)].

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | TargetID | C1 | N1 | C2 | N2 | C3 | N3 | C4 | N4 | C5 | N5 | C6 | N6 | Effect Size | Pvalue | Methylation Rate |
| NTSR1 | cg03567830 | 0.152 | 0.147 | 0.335 | 0.155 | 0.252 | 0.179 | 0.247 | 0.110 | 0.188 | 0.082 | 0.457 | 0.140 | 0.136 | 0.013 | 16.7% |
| SLC5A8 | cg05722918 | 0.201 | 0.052 | 0.057 | 0.064 | 0.041 | 0.085 | 0.032 | 0.041 | 0.072 | 0.038 | 0.393 | 0.028 | 0.081 | 0.127 | 16.7% |
| GALR1 | cg15343119 | 0.572 | 0.154 | 0.195 | 0.257 | 0.608 | 0.220 | 0.581 | 0.194 | 0.215 | 0.102 | 0.679 | 0.142 | 0.297 | 0.011 | 66.7% |
| AGTR1 | cg20530314 | 0.137 | 0.072 | 0.091 | 0.165 | 0.099 | 0.038 | 0.524 | 0.085 | 0.061 | 0.033 | 0.251 | 0.065 | 0.117 | 0.084 | 16.7% |

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