|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author/year** | **Type of Cancer** | **Epigenetic alteration** | **Results**  | **Mechanisms**  | **comments** |
| Liu C-C et al. , 2015  | Lung Cancer | IL-6 increased DNMT1🡪methylation of cancer suppressor gene p53 and p21 in A549 cancer cells | Cancer up-regulated | inflammatory cytokines in microenviroment🡪 cancer progress | 1. In vitro study:lung cancer stem cells vs. IL-6 enrichment
2. IL-6 is also expressed in metabolic inflammation.
 |
| Yu Z et al. , 2015 | Breast cancer (BrCa)  | DNMT1 expression higher in BrCa than fibroadenoma | Increase lymph node metastasis; shorter disease-free survival  | DNMT1 🡪 promoter hypermethylation | 1. Human, longitudinal study
2. Potential causal
 |
| Zheng Y et al., 2015 | Hepatocellular carcinoma (HCC) | Histone de-Acetylation in cancer vs adjacent tissues | Hepatocellular Cancer down regulated | histone deacetylase (HDAC) increased the level of miR-376a (cancer suppressor) | 1. In vitro study
2. No causal inference
 |
| Karczmarski J et al., 2014 | Colorectal Cancer (CRC) | Histone acetylationin CRC tissues and healthy mucosa samples | Histone (H3) acetylation is upregulated in CRC, | Proteomic approach for the detection of histone modifications at a global scale. | 1. In vitro study
2. No causal inference
 |

Supplemental Table1a. Selected examples of epigenetic modification and cancer

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Table 2a. (Supplemental) The role of microRNAs and cancer relationship

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| --- | --- | --- | --- | --- | --- |
| **Author/year** | **Type of Cancer** | **miRNAs involved** | **Methods**  | **Results**  | **comments** |
| Kent OA et al. 2016 | Pancreatic and colorectal Cancer | miR-31 plus KRAS mutations | In patient derived xenografts and a panel of pancreatic and colorectal cancer cells, miR-31 promoter in a MAPK-dependent manner  | Invasion and migration of multiple pancreatic cancer cells | 1. *In vitro* study
2. Mechanism study without comparison
 |
| Hung KF et al 2016 | Oral potential malignancies ( OPMD) | miR-31upregulation | Saliva samples and tissue samples from OPMD patients followed 820days | Malignant transformation 🡪 increased expression of miR-31 | 1. Human, longitudinal study
2. Potential causal
3. miR-31 is the cause or just a mechanism?
 |
| Sun Y et al. 2015 | Esophageal Cancer | miR-204 | Expression level of miR-204 in primary EC cases and cell lines by quantitative Real-Time PCR | miR-204 inhibited epithelial-mesenchymal transition🡪cancer down regulation | 1. *In vitro* study
2. No causal inference
 |
| Shi W et al 2015 | Oral squamous cell carcinoma | miR-375 | MicroRNA and mRNA profiling in oral lichen planus (OLP), oral squamous cell carcinoma (OSCC), and normal tissue from the same patients. | 1. miR-375 decreased in tissues with malignant transformation
2. miR-375 may be oncosuppressors.
 | 1. *In vitro* study
2. No causal inference
 |
| Lerner et al 2015 | Head and neck squamous cell carcinoma | miR-146a & miR-155 | HNSCC patients (N=12) and sex- and age-matched controls (N=12) | 1. No diff at baseline miR profile
2. In patients: down-regulation of miR-146a and miR-155 🡪 distant metastasis
 | 1. Human, longitudinal study
2. Potentially causal
3. miR-146a and miR-155 may be oncosuppressors.
 |
| Shi XM et al 2015 | hepatocellular carcinoma | lncRNA Sox2ot  | Tumor and adjacent non-tumor tissues | High lncRNA Sox2ot expression🡪 shorter survival | 1. Human, longitudinal study
2. lncRNA Sox2ot expression may be oncogenic
 |
| Chen X et al 2015 | Uterine Cervix squamous cell cancer | lncRNA CCAT2 | Cancer to the adjacent non-tumor tissues | High expression of lncRNA CCAT2 correlated with invasiveness of tumor and poor survival | 1. Human, longitudinal study
2. lncRNA CCAT2 may be onco-enhancer.
 |
| Zhang S et al 2015 | Oral squamous cell carcinoma | lncRNA profile | Samples from OSCC 57 patient vs normal gene from data base (N=22) | FTH1P3, PDIA3F and GTF2IRD2P1 targeted MMP1, MMP3, MMP9, PLAU (plasminogen activator, urokinase) and IL8. | 1. Cross-sectional in vitro study
2. lncRNA , the cause or just a mechanism?
 |
| Wu J et al 2015 | Oral squamous cell carcinoma (OSCC) | RNA-HOX transcript antisense intergenic RNA (HOTAIR) | surgically resected tumor tissue (N= 50) vs. paracancerous tissues | HOTAIR was highly expressed in OSCC tissues and facilitated the growth of OSCC cells.  | 1. Blocking HOTAIR expression 🡪decelerated cell growth suggests potential causality.
 |
| Wu Y et al 2015 | Oral squamous cell carcinoma (OSCC) | lncRNA HOTAIR | OSCC vs. non-tumor tissue | 1. HOTAIR expression increased in OSCC.
2. HOTAIR🡪 poor survival
 | 1. Negative correlation HOTAIR and E-cadherin levels.
 |

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