**Таблица 1.** Распределение больных злокачественными опухолями яичников в зависимости от гистологического варианта строения опухоли

|  |  |
| --- | --- |
| Гистологический вариант | Частота, абс. (%) |
| Серозная аденокарцинома | 44 (47,3) |
| Серозная цистаденокарцинома | 38 (40,9) |
| Муцинозная цистаденокарцинома | 1 (1,0) |
| Эндометриоидная аденокарцинома | 10 (10,8) |

**Table 1.** Distribution of the patients with malignant ovarian tumors depending on the histological type of the tumor

|  |  |
| --- | --- |
| Histological type | Frequency, N (%) |
| Serous adenocarcinoma | 44 (47.3) |
| Serous cystadenocarcinoma | 38 (40.9) |
| Mucinous cystadenocarcinoma | 1 (1.0) |
| Endometrioid adenocarcinoma | 10 (10.8) |

**Таблица 2.** Данные анализа метилирования генов микроРНК в образцах ткани яичников разных групп больных и группы контроля

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Ген *MIR* | Метилирование в ткани яичников, Ме [Q1; Q3], min–max, % | | | Значение *p*\* (FDR = 0,01) |
| Контроль (n = 15) | Ткань опухоли яичников | |
| ПОЯ (n = 6) | ЗОЯ (n = 93) |
| *124-1* | 0,5 [0,2; 3,1], 0,1–9,2 | 14,0 [8,9; 24,0], 8,8–45,0 | 10,0 [2,6; 21,6], 0–67,3 | p0–2 < 0,0001  p0–1 = 0,003 |
| *124-2* | 7,4 [0,2; 13,1], 0,1–19,5 | 19,0 [11,0; 36,5], 6,4–92,3 | 29,0 [6,8; 51,7], 0–98,1 | p0–2 = 0,0017 |
| *124-3* | 4,7 [0,3; 8,9], 0,1–17,8 | 16,8 [12,7; 30,9], 9,6–34,6 | 21,4 [8,5; 41,7], 0,04–95,3 | p0–2 < 0,0001 |
| *125B-1* | 5,6 [1,6; 11,4], 1,1–16,2 | 36,6 [1,5; 75,1], 0,4–97,3 | 34,8 [11,2; 60,6], 0,1–99,3 | p0–2 < 0,0001 |
| *127* | 8,8 [0,9; 11,1]; 0,2–18,8 | 12,7 [1,6; 20,4], 1,0–31,0 | 27,6 [4,8; 53,9], 0,08–93,3 | p0–2 < 0,001 |
| *129-2\*\** | 8,2 [4,9; 11,2], 4,3–13,3 | 51,6 [12,7; 87,4], 2,1–89,0 | 31,2 [10,3; 51,5], 0,3–99,3 | p0–2 < 0,001  p0–1 = 0,036 |
| *132\*\** | 1,3 [0,1; 4,3], 0,1–9,0 | 25,6 [7,6; 47,2], 0,2–62,5 | 9,8 [3,6; 31,9], 0,05–98,8 | p0–2 < 0,0001  p0–1 = 0,008 |
| *137* | 7,5 [2,9; 10,0], 0,3–13,2 | 22,9 [1,8–76,7], 1,0–90,0 | 31,1 [2,5; 56,9], 0–98,5 | p0–2 = 0,018 |
| *148A\*\** | 5,0 [3,0; 10,9], 0,1–13,6 | 31,3 [25,0; 50,0], 9,9–90,8 | 7,9 [1,9; 28,7], 0–94,4 | p0–1 = 0,018  p1–2 = 0,047 |
| *191* | 28,5 [13,8; 32,9], 8,6–94,4 | 4,8 [1,8; 22,2], 1,7–33,8 | 7,0 [2,4; 25,8], 0,01–90,7 | p0–2 = 0,006 |
| *193A* | 4,5 [0,3; 7,3], 0,1–12,2 | 32,1 [8,5; 38,3], 0,1–53,1 | 34,8 [15,4; 56,4], 0,1–98,4 | p0–2 < 0,0001 |
| *203\*\** | 6,9 [0,9; 9,9], 0,1–15,2 | 13,8 [0,6; 74,5], 0,2–90,9 | 6,8 [1,3; 35,3], 0,01–98,2 | – |
| *212* | 4,6 [1,6; 8,3], 0,2–13,9 | 5,9 [0,4; 17,8], 0,03–70,5 | 4,8 [1,5; 12,6], 0,02–98,2 | – |
| *34B/C* | 0,9 [0,4; 1,7], 0,1–7,7 | 21,3 [11,4; 27,4], 3,7–76,2 | 17,6 [3,1; 35,4], 0,01–98,1 | p0–2 < 0,0001  p0–1 = 0,005 |
| *375* | 1,0 [0,2; 2,8], 0,1–9,1 | 7,8 [2,2; 15,0], 0,01–28,2 | 10,9 [3,2; 34,2], 0–92,5 | p0–2 < 0,001 |
| *9-1* | 2,0 [1,4; 4,0], 0,1–8,8 | 7,3 [4,0; 10,0], 0,05–94,6 | 24,4 [7,7; 56,3], 0,01–93,6 | p0–2 < 0,0001 |
| *9-3* | 7,4 [5,2; 14,9], 0–18,0 | 10,7 [5,4; 24,8], 2,1–36,5 | 21,9 [7,2; 36,4], 0,02–98,3 | p0–2 = 0,014 |
| *130B* | 1,6 [0,3; 2,9], 0–7,2 | 7,8 [1,6; 28,2], 1,4–91,4 | 16,9 [6,8; 32,5], 0,1–99,1 | p0–2 < 0,0001 |
| *107\*\** | 7,2 [2,4; 10,2], 1,6–17,4 | 26,1 [18,2; 31,1], 3,5–92,3 | 15,7 [6,2; 53,5], 0–93,0 | p0–2 = 0,024 |
| *1258\*\** | 1,0 [0,3; 12,2], 0,2–14,1 | 35,6 [17,0; 62,2], 4,2–70,2 | 11,2 [4,4; 40,8], 0,1–90,8 | p0–2 < 0,001  p0–1 = 0,002 |
| *339* | 7,9 [3,2; 9,4], 1,2–11,8 | 23,6 [9,2; 48,1], 8,2–99,9 | 21,2 [8,2; 54,3], 0,2–99,7 | p0–2 < 0,001  p0–1 = 0,009 |

FDR – false discovery rate, ожидаемая доля ложных отклонений, ЗОЯ – злокачественные опухоли яичников; ПОЯ – пограничные опухоли яичников

p0–1 – различия между группой контроля и группой больных ПОЯ, p0–2 – различия между группой контроля и группой больных ЗОЯ, p1–2 – различия между группой больных ПОЯ и группой больных ЗОЯ

\* Представлены только статистически значимые различия

\*\* Гены, у которых значения медиан существенно выше в ПОЯ, чем в ЗОЯ

**Table 2.** Analysis of the miRNA gene methylation in the tissue samples from various patient groups and the control group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| *MIR* gene | Methylation in the ovarian tissue, Ме [Q1; Q3], Min–Max, % | | | *P* value\* (FDR = 0.01) |
| Control (n = 15) | Ovarian tumor tissue | |
| BOT (n = 6) | MOT (n = 93) |
| *124-1* | 0.5 [0.2; 3.1], 0.1–9.2 | 14.0 [8.9; 24.0], 8.8–45.0 | 10.0 [2.6; 21.6], 0–67.3 | p0–2 < 0.0001  p0–1 = 0.003 |
| *124-2* | 7.4 [0.2; 13.1], 0.1–19.5 | 19.0 [11.0; 36.5], 6.4–92.3 | 29.0 [6.8; 51.7], 0–98.1 | p0–2 = 0.0017 |
| *124-3* | 4.7 [0.3; 8.9], 0.1–17.8 | 16.8 [12.7; 30.9], 9.6–34.6 | 21.4 [8.5; 41.7], 0.04–95.3 | p0–2 < 0.0001 |
| *125B-1* | 5.6 [1.6; 11.4], 1.1–16.2 | 36.6 [1.5; 75.1], 0.4–97.3 | 34.8 [11.2; 60.6], 0.1–99.3 | p0–2 < 0.0001 |
| *127* | 8.8 [0.9; 11.1]; 0.2–18.8 | 12.7 [1.6; 20.4], 1.0–31.0 | 27.6 [4.8; 53.9], 0.08–93.3 | p0–2 < 0.001 |
| *129-2\*\** | 8.2 [4.9; 11.2], 4.3–13.3 | 51.6 [12.7; 87.4], 2.1–89.0 | 31.2 [10.3; 51.5], 0.3–99.3 | p0–2 < 0.001  p0–1 = 0.036 |
| *132\*\** | 1.3 [0.1; 4.3], 0.1–9.0 | 25.6 [7.6; 47.2], 0.2–62.5 | 9.8 [3.6; 31.9], 0.05–98.8 | p0–2 < 0.0001  p0–1 = 0.008 |
| *137* | 7.5 [2.9; 10.0], 0.3–13.2 | 22.9 [1.8–76.7], 1.0–90.0 | 31.1 [2.5; 56.9], 0–98.5 | p0–2 = 0.018 |
| *148A\*\** | 5.0 [3.0; 10.9], 0.1–13.6 | 31.3 [25.0; 50.0], 9.9–90.8 | 7.9 [1.9; 28.7], 0–94.4 | p0–1 = 0.018  p1–2 = 0.047 |
| *191* | 28.5 [13.8; 32.9], 8.6–94.4 | 4.8 [1.8; 22.2], 1.7–33.8 | 7.0 [2.4; 25.8], 0.01–90.7 | p0–2 = 0.006 |
| *193A* | 4.5 [0.3; 7.3], 0.1–12.2 | 32.1 [8.5; 38.3], 0.1–53.1 | 34.8 [15.4; 56.4], 0.1–98.4 | p0–2 < 0.0001 |
| *203\*\** | 6.9 [0.9; 9.9], 0.1–15.2 | 13.8 [0.6; 74.5], 0.2–90.9 | 6.8 [1.3; 35.3], 0.01–98.2 | – |
| *212* | 4.6 [1.6; 8.3], 0.2–13.9 | 5.9 [0.4; 17.8], 0.03–70.5 | 4.8 [1.5; 12.6], 0.02–98.2 | – |
| *34B/C* | 0.9 [0.4; 1.7], 0.1–7.7 | 21.3 [11.4; 27.4], 3.7–76.2 | 17.6 [3.1; 35.4], 0.01–98.1 | p0–2 < 0.0001  p0–1 = 0.005 |
| *375* | 1.0 [0.2; 2.8], 0.1–9.1 | 7.8 [2.2; 15.0], 0.01–28.2 | 10.9 [3.2; 34.2], 0–92.5 | p0–2 < 0.001 |
| *9-1* | 2.0 [1.4; 4.0], 0.1–8.8 | 7.3 [4.0; 10.0], 0.05–94.6 | 24.4 [7.7; 56.3], 0.01–93.6 | p0–2 < 0.0001 |
| *9-3* | 7.4 [5.2; 14.9], 0–18.0 | 10.7 [5.4; 24.8], 2.1–36.5 | 21.9 [7.2; 36.4], 0.02–98.3 | p0–2 = 0.014 |
| *130B* | 1.6 [0.3; 2.9], 0–7.2 | 7.8 [1.6; 28.2], 1.4–91.4 | 16.9 [6.8; 32.5], 0.1–99.1 | p0–2 < 0.0001 |
| *107\*\** | 7.2 [2.4; 10.2], 1.6–17.4 | 26.1 [18.2; 31.1], 3.5–92.3 | 15.7 [6.2; 53.5], 0–93.0 | p0–2 = 0.024 |
| *1258\*\** | 1.0 [0.3; 12.2], 0.2–14.1 | 35.6 [17.0; 62.2], 4.2–70.2 | 11.2 [4.4; 40.8], 0.1–90.8 | p0–2 < 0.001  p0–1 = 0.002 |
| *339* | 7.9 [3.2; 9.4], 1.2–11.8 | 23.6 [9.2; 48.1], 8.2–99.9 | 21.2 [8.2; 54.3], 0.2–99.7 | p0–2 < 0.001  p0–1 = 0.009 |

BOT, borderline ovarian tumors; FDR, false discovery rate, an expected proportion of false positive abnormalities; MOT, malignant ovarian tumors

p0–1, the difference between the control group and the BOT group; p0–2, the difference between the control group and the MOT group; p1–2, the difference between the BOT and the MOT groups

\* Only significant difference is given

\*\* The genes with median values substantially higher in BOT, than in MOT

**Таблица 3.** Метилирование группы генов миРНК в образцах злокачественных опухолей яичников в зависимости от гистологического варианта строения опухоли

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Ген *MIR* | Метилирование в опухолевой ткани яичников, Ме [Q1; Q3], % | | | |
| Гистологический вариант строения опухоли | | | |
| САК (n = 44) | СЦАК (n = 38) | ЭАК (n = 10) | МЦАК (n = 1) |
| *124-1* | 11,4 [3,3; 21,0] | 10,0 [2,6; 30,0] | 3,8 [0,4; 21,2] | 2,1 |
| *124-2* | 42,0 [7,2; 66,7] | 21,2 [6,8; 37,2] | 11,7 [3,0; 41,2] | 0 |
| *124-3* | 21,3 [11,9; 35,8] | 18,8 [4,8; 50,3] | 28,8 [8,6; 39,8] | 52,7 |
| *125B-1* | 32,8 [11,2; 57,6] | 35,5 [13,0; 69,1] | 33,4 [11,2; 85,0] | 7,1 |
| *127* | 35,9 [5,1; 56,1] | 18,8 [3,9; 45,0] | 34,5 [18,2; 45,1] | 54,3 |
| *129-2* | 32,1 [7,6; 46,6] | 39,4 [12,5; 84,3] | 23,0 [15,2; 31,2] | 2,9 |
| *132* | 9,4 [4,5; 16,9] | 11,5 [3,6; 57,3] | 11,7 [1,9; 35,3] | 0,1 |
| *137* | 36,6 [8,0; 53,1] | 33,3 [2,0; 60,1] | 12,7 [1,0; 64,4] | 2,3 |
| *148A\** | 11,4 [5,9; 34,9] | 2,4 [1,1; 10,1] | 30,4 [7,2; 45,8] | 1,9 |
| *191\** | 14,7 [4,9; 28,8] | 2,4 [0,7; 7,0] | 32,0 [11,2; 42,0] | 21,3 |
| *193A* | 27,6 [14,5; 54,3] | 42,3 [9,0; 59,7] | 38,7 [24,9; 66,4] | 34,6 |
| *203А* | 6,1 [0,9; 33,7] | 10,3 [2,6; 40,9] | 3,0 [1,0; 37,6] | 1,3 |
| *212* | 8,7 [1,6; 13,6] | 2,9 [1,1; 7,4] | 9,5 [0,5; 31,1] | 2,6 |
| *34B/C* | 12,7 [3,8; 29,8] | 23,1 [2,3; 49,2] | 11,2 [1,3; 15,7] | 31,3 |
| *375* | 9,8 [0,5; 36,7] | 11,3 [4,3; 37,6] | 10,8 [8,1; 18,0] | 1,6 |
| *9-1* | 25,6 [10,6; 53,8] | 38,2 [3,0; 63,6] | 20,0 [2,2; 24,2] | 2,0 |
| *9-3\*\** | 15,8 [5,9; 23,9] | 31,3 [13,5; 52,2] | 16,0 [4,6; 45,1] | 3,1 |
| *130B* | 16,1 [7,3; 23,9] | 22,2 [6,8; 48,2] | 15,1 [4,5; 39,0] | 1,9 |
| *107* | 10,5 [5,8; 56,9] | 22,2 [6,2; 44,5] | 26,3 [8,3; 59,2] | 2,7 |
| *1258\*\** | 8,2 [3,9; 27,2] | 25,1 [7,1; 56,2] | 5,0 [3,5; 8,0] | 27,2 |
| *339* | 18,7 [2,7; 49,3] | 21,1 [11,2; 59,1] | 22,0 [12,0; 26,5] | 44,6 |

МЦАК – муцинозная цистаденокарцинома, САК – серозная аденокарцинома, СЦАК – серозная цистаденокарцинома, ЭАК – эндометриоидная аденокарцинома

\* p < 0,001, FDR (false discovery rate, ожидаемая доля ложных отклонений) = 0,01

\*\* p < 0,05, FDR (false discovery rate, ожидаемая доля ложных отклонений) = 0,01

**Table 3.** Methylation of the miRNA gene group in the malignant ovarian tumor tissue depending on the histological type of the tumor

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| *MIR* gene | Methylation in the ovarian tumor tissue, Ме [Q1; Q3], % | | | |
| Histological type of the tumor | | | |
| SAC (n = 44) | SCAC (n = 38) | EAC (n = 10) | MCAC (n = 1) |
| *124-1* | 11.4 [3.3; 21.0] | 10.0 [2.6; 30.0] | 3.8 [0.4; 21.2] | 2.1 |
| *124-2* | 42.0 [7.2; 66.7] | 21.2 [6.8; 37.2] | 11.7 [3.0; 41.2] | 0 |
| *124-3* | 21.3 [11.9; 35.8] | 18.8 [4.8; 50.3] | 28.8 [8.6; 39.8] | 52.7 |
| *125B-1* | 32.8 [11.2; 57.6] | 35.5 [13.0; 69.1] | 33.4 [11.2; 85.0] | 7.1 |
| *127* | 35.9 [5.1; 56.1] | 18.8 [3.9; 45.0] | 34.5 [18.2; 45.1] | 54.3 |
| *129-2* | 32.1 [7.6; 46.6] | 39.4 [12.5; 84.3] | 23.0 [15.2; 31.2] | 2.9 |
| *132* | 9.4 [4.5; 16.9] | 11.5 [3.6; 57.3] | 11.7 [1.9; 35.3] | 0.1 |
| *137* | 36.6 [8.0; 53.1] | 33.3 [2.0; 60.1] | 12.7 [1.0; 64.4] | 2.3 |
| *148A\** | 11.4 [5.9; 34.9] | 2.4 [1.1; 10.1] | 30.4 [7.2; 45.8] | 1.9 |
| *191\** | 14.7 [4.9; 28.8] | 2.4 [0.7; 7.0] | 32.0 [11.2; 42.0] | 21.3 |
| *193A* | 27.6 [14.5; 54.3] | 42.3 [9.0; 59.7] | 38.7 [24.9; 66.4] | 34.6 |
| *203А* | 6.1 [0.9; 33.7] | 10.3 [2.6; 40.9] | 3.0 [1.0; 37.6] | 1.3 |
| *212* | 8.7 [1.6; 13.6] | 2.9 [1.1; 7.4] | 9.5 [0.5; 31.1] | 2.6 |
| *34B/C* | 12.7 [3.8; 29.8] | 23.1 [2.3; 49.2] | 11.2 [1.3; 15.7] | 31.3 |
| *375* | 9.8 [0.5; 36.7] | 11.3 [4.3; 37.6] | 10.8 [8.1; 18.0] | 1.6 |
| *9-1* | 25.6 [10.6; 53.8] | 38.2 [3.0; 63.6] | 20.0 [2.2; 24.2] | 2.0 |
| *9-3\*\** | 15.8 [5.9; 23.9] | 31.3 [13.5; 52.2] | 16.0 [4.6; 45.1] | 3.1 |
| *130B* | 16.1 [7.3; 23.9] | 22.2 [6.8; 48.2] | 15.1 [4.5; 39.0] | 1.9 |
| *107* | 10.5 [5.8; 56.9] | 22.2 [6.2; 44.5] | 26.3 [8.3; 59.2] | 2.7 |
| *1258\*\** | 8.2 [3.9; 27.2] | 25.1 [7.1; 56.2] | 5.0 [3.5; 8.0] | 27.2 |
| *339* | 18.7 [2.7; 49.3] | 21.1 [11.2; 59.1] | 22.0 [12.0; 26.5] | 44.6 |

EAC, endometrioid adenocarcinoma; MCAC, mucinous cystadenocarcinoma; SAC, serous adenocarcinoma; SCAC, serous cystadenocarcinoma

\* p < 0.001, FDR (false discovery rate, an expected proportion of false positive abnormalities) = 0.01

\*\* p < 0.05, FDR (false discovery rate, an expected proportion of false positive abnormalities) = 0.01