**Changes over time in the HSPs, MMPs and TIMP1 marker content on CD9-positive and FABP4-positive extracellular vesicles at various steps of thermoradiochemotherapy and after it**

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| --- | --- | --- | --- | --- | --- |
| **Extracellular vesicle population** | **The marker content (%) at control timepoints** | | | | **P** |
| **1** | **2** | **3** | **4** |
| CD9+ | | | | | |
| HSP60+ | 22.4 [9.25; 30.7] | 13.7 [10.7; 14.6] | 25.0 [15.2; 62.0] | 10.6 [9.06; 11.5] | 0.085 |
| HSP60+27+90- | 15.0 [3.84; 25.7] | 19.9 [11.7; 32.1] | 2.77 [0.34; 38.8] | 17.5 [12.5; 37.5] | 0.166 |
| HSP60+27-90- | 84.86 [73.9; 95.8] | 74.7 [67.8; 88.2] | 96.8 [60.6; 99.6] | 82.2 [56.7; 87.1] | 0.171 |
| MMP2+ | 3.84 [2.71; 4.29] | 4.12 [2.46; 6.27] | 3.66 [2.55; 5.36] | 3,79 [2.0; 5.60] | 0.801 |
| MMP2+9+TIMP1+ | 10.8 [0.54; 17.6] | 0.29 [0.14; 16.7] | 8.90 [0.35; 15.4] | 6,23 [0,89; 15,6] | 0.539 |
| MMP2+9+TIMP1- | 10.8 [3.14; 17.2] | 2.03 [1.45; 14.3] | 4.19 [0.97; 15.1] | 7,59 [3.475; 16.4] | 0.614 |
| MMP2+9-TIMP1+ | 14.9 [10.3; 16.6] | 14.5 [8.54; 19.0] | 13.8 [12.9; 22.6] | 17,3 [12.4; 21.3] | 0.213 |
| MMP9+ | 5.52 [4.43; 7.75] | 3.00 [2.23; 3.19] | 3.08 [2.41; 4.57] | 3,59 [3.07; 5.07] | 0.045 |
| MMP9+2-TIMP1+ | 15.9 [6.71; 26.0] | 6.82 [4.58; 18.0] | 7.13 [5.42; 15.2] | 9,36 [6.29; 11.2] | 0.048 |
| FABP4+ | | | | | |
| HSP60+ | 26.0 [18.2; 37.5] | 31.6 [17.6; 41.3] | 38.2 [30.6; 63.0] | 22.2 [18.5; 29.9] | 0.012 |
| HSP60+27+90- | 13.3 [9.33; 28.5] | 10.7 [8.25; 23.0] | 7.34 [1.02; 30.2] | 6.27 [4.44; 12.5] | 0.146 |
| HSP60+27-90- | 86.6 [71.3; 90.1] | 89.1 [76.9; 91.4] | 92.5 [69.7; 98.9] | 93.5 [87.3; 95.5] | 0.843 |
| MMP2+ | 6.73 [5.01; 17.98] | 7.995 [5.275; 15.8] | 7.75 [5.69; 16.29] | 8.33 [6.12; 8.73] | 0.764 |
| MMP2+9+TIMP1+ | 4.49 [0.23; 5.85] | 4.065 [0.095; 5.82] | 4.64 [0.29; 6.45] | 3.68 [0.17; 3.78] | 0.567 |
| MMP2+9+TIMP1- | 1.83 [1.27; 2.77] | 2.685 [0.73; 4.735] | 1.89 [1.18; 4.0] | 1.36 [0.72; 1.96] | 0.543 |
| MMP2+9-TIMP1+ | 21.4 [16.4; 34.7] | 21.3 [16.6; 26.5] | 24.4 [11.8; 36.4] | 22.7 [10.4; 23.2] | 0.631 |
| MMP9+ | 1.39 [1.06; 7.13] | 1.66 [1.255; 5.39] | 1.79 [1.38; 6.89] | 1.69 [1.5; 3.34] | 0.321 |
| MMP9+2-TIMP1+ | 5.66 [3.65; 8.07] | 4.24 [2.87; 6.92] | 7.99 [5.71; 9.91] | 5.58 [5.34; 6.22] | 0.124 |

Control timepoints: 1, at baseline; 2, in the middle of the thermoradiochemotherapy (TRCT) course; 3, at 6 to 10 weeks after the end of TRCT; 4, at 6 months after timepoint 1

P, the significance of the variation by Friedman test

The values are given as medians and interquartile ranges (Ме [Q1; Q3]) for proportions (%)