

Table S1. Patients' and tumor's characteristics. Gleason score, enzalutamide treatment (ENZ), docetaxel treatment (DCX), cabazitaxel treatment (CBX), abiraterone acetate treatment period (AA duration), objective response to AA treatment (OR), PSA levels changes after AA treatment (PSA), progression free survival after AA treatment (PFS). AA = abiraterone acetate; MR = mixed response; NE = not evaluable; DP = disease progression; PR = partial response; S = PSA stabilization; SD = stable disease; UNK = unknown; <50% = PSA reduction less than 50% compared to baseline; >50% = PSA reduction more than 50% compared to baseline; Y=yes ; N=no. In bold, the patients used for the Exiqon panel analysis.

| | Patient code | Age | Gleason Score | ENZ | DCX | CBX | AA Duration (months) | OR | PSA | PFS (months) |
|----------------|--------------|-----|---------------|-----|-----|-----|----------------------|-------|------|--------------|
| Non-responders | P1 | 75 | 8 | Y | Y | Y | 3.93 | DP | <50% | 3.9 |
| | P2 | 84 | 7 | Y | Y | N | 2.93 | NE | <50% | 2.7 |
| | P3 | 85 | 8 | N | Y | N | 4.03 | DP | <50% | 3.7 |
| | P4 | 78 | 9 | Y | Y | Y | 6.8 | MR | <50% | 5.4 |
| | P5 | 75 | 8 | Y | Y | Y | 3.77 | DP | <50% | 3.7 |
| | P6 | 80 | 8 | N | Y | N | 3.73 | DP | S | 3.7 |
| | P7 | 73 | 7 | Y | Y | N | 2.47 | NE | <50% | 2.4 |
| | P8 | 78 | 7 | N | Y | N | 1.93 | NE | <50% | 1.9 |
| | P9 | 77 | 8 | Y | Y | N | 3.97 | DP | >50% | 3.9 |
| | P10 | 76 | UNK | Y | Y | Y | 3.87 | DP | <50% | 3.8 |
| | P11 | 64 | 9 | Y | Y | Y | 4.8 | DP | >50% | 4.7 |
| | P12 | 74 | 9 | Y | Y | N | 4.63 | NE | <50% | 4.2 |
| | P13 | 78 | 7 | N | Y | N | 3.27 | DP | <50% | 3.7 |
| | P14 | 68 | 8 | N | Y | Y | 5.57 | MR | <50% | 5.5 |
| | P15 | 46 | 9 | Y | Y | Y | 4.63 | MR | >50% | 4.6 |
| | P16 | 75 | 9 | N | Y | N | 13.1 | DP | >50% | 1.8 |
| | P17 | 70 | 8 | N | Y | N | 4.7 | DP | <50% | 4.6 |
| | P18 | 63 | 10 | N | Y | N | 3.73 | DP | >50% | 3.7 |
| | P19 | 82 | 6 | N | Y | N | 3.93 | DP | <50% | 3.9 |
| | P20 | 76 | 9 | Y | Y | N | 2.67 | DP | <50% | 3.9 |
| | P21 | 70 | 10 | N | Y | Y | 5.6 | DP | >50% | 5.5 |
| Responders | P22 | 70 | 9 | N | Y | Y | 12.17 | PR | <50% | 12 |
| | P23 | 84 | 7 | N | Y | N | 4.67 | PR | >50% | 16.6 |
| | P24 | 73 | 7 | N | Y | Y | 20.8 | PR | >50% | 20.8 |
| | P25 | 81 | 7 | N | Y | N | 9.13 | PR | <50% | 9 |
| | P26 | 75 | 7 | N | Y | N | 13.37 | PR | <50% | 13.2 |
| | P27 | 74 | 9 | N | Y | N | 21.33 | PR | >50% | 21.7 |
| | P28 | 76 | 6 | Y | Y | Y | 15.1 | SD/PR | >50% | 14.9 |
| | P29 | 80 | 9 | N | Y | N | 9.33 | PR | >50% | 8.7 |
| | P30 | 70 | 9 | N | Y | Y | 7.5 | MR | S | 7.8 |
| | P31 | 72 | UNK | N | Y | Y | 14.3 | PR | >50% | 13.1 |
| | P32 | 84 | UNK | N | N | N | 21.7 | PR | >50% | 21.7 |
| | P33 | 73 | 9 | Y | Y | Y | 4.43 | PR | >50% | 14.8 |

Table S2. Fold change and literature review of miRNAs candidates.

| miRNA | Fold Change (NR vs. R) | Literature Review |
|-------------|------------------------|-------------------|
| miR-103a-3p | 1.1 | [1–4] |
| miR-144-3p | -4.1 | [5–8] |
| miR-182-5p | 4.9 | [9–11] |
| miR-29b-3p | -2.2 | [12,13] |
| miR-331-5p | 6.9 | [14] |
| miR-33a-5p | -4.7 | [15,16] |
| miR-363-3p | -2.4 | [17–19] |
| miR-378a-5p | -4.7 | [20–24] |

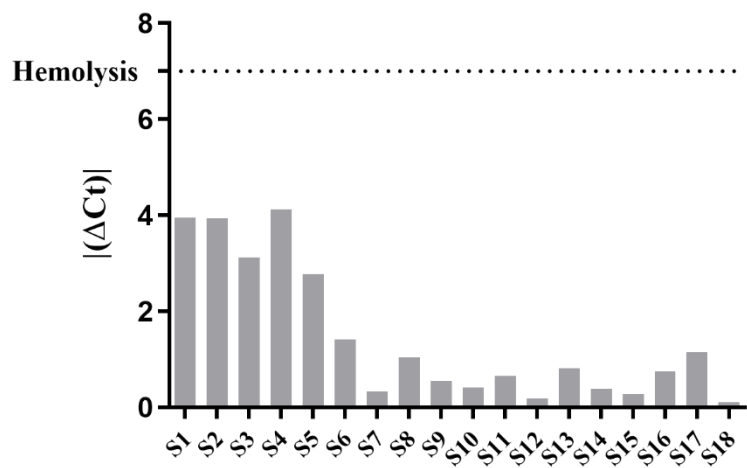


Figure S1. Hemolysis check for Exiqon miRNome panels data. The absolute difference among Ct values of miR-451a-5p and miR-23a-3p indicates that no hemolysis was present in the samples analyzed following the criteria of Blondal et al. ($\Delta Ct > 7$) [25].

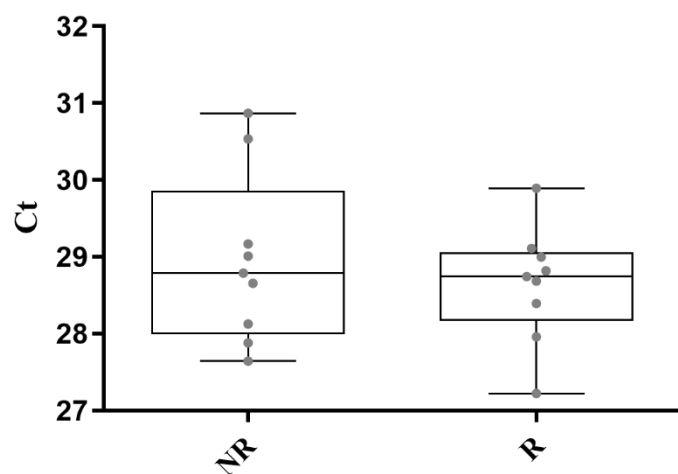


Figure S2. Ct values of miR-425-5p in candidate analysis, in non-responder (NR) and responder patients (R).

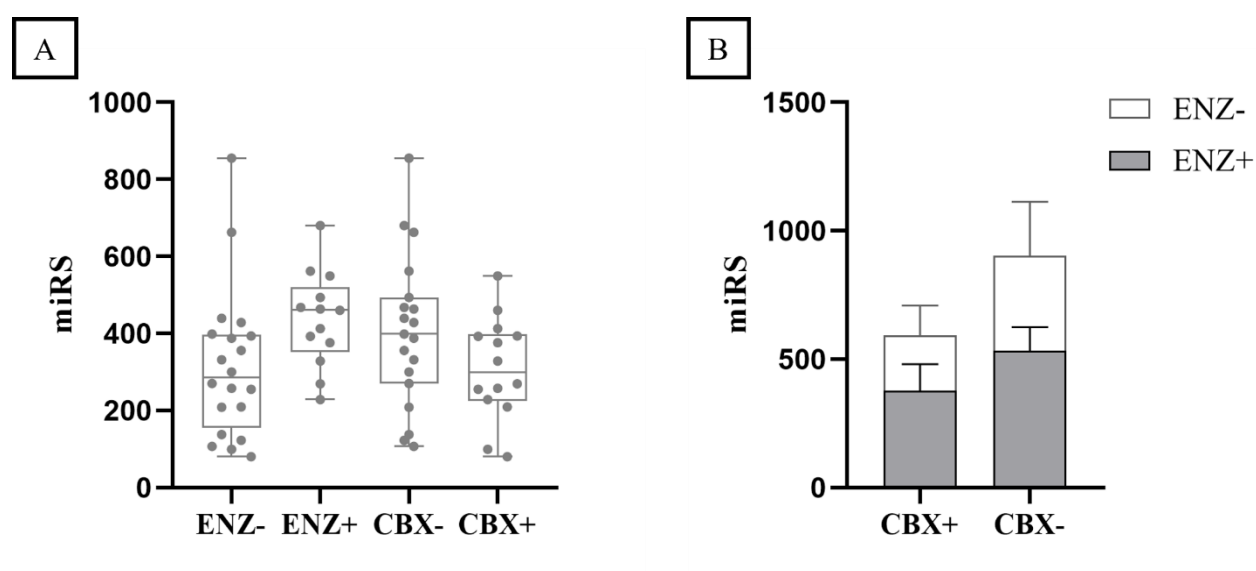


Figure S3. (A) Patients were grouped based on miRS data for enzalutamide and cabazitaxel treatment. The Student's T-test (ENZ- vs ENZ+ and CBX- vs CBX+) did not show significant differences. (B) Patients were also grouped based on miRS for combined treatment of enzalutamide and cabazitaxel. The 2-way ANOVA did not show significant interactions.

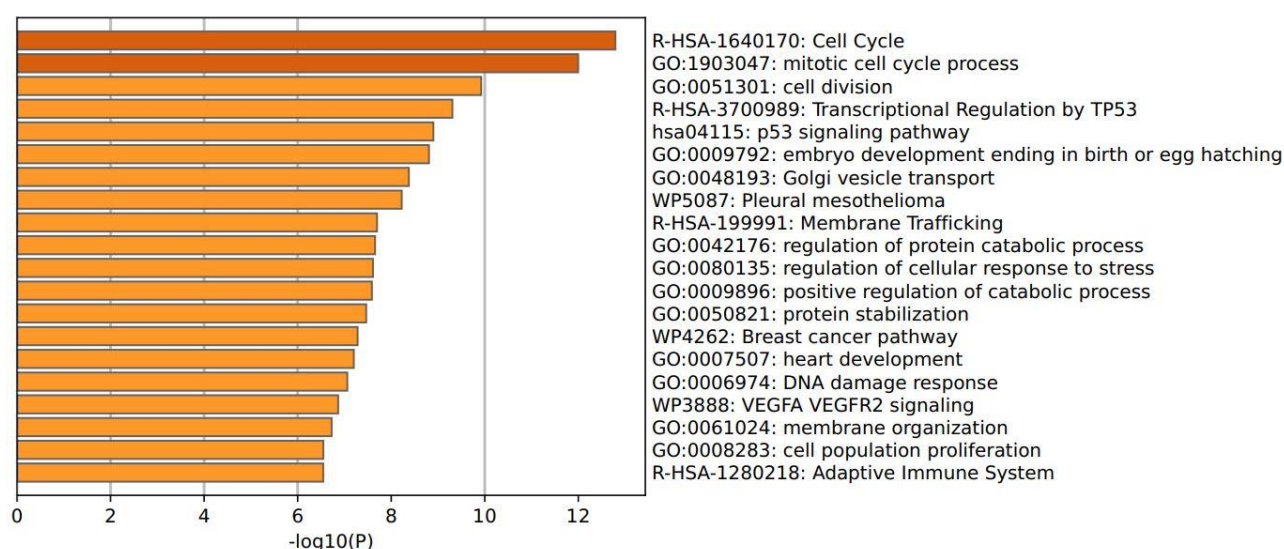


Figure S4. Gene ontology analysis (Metascape) on shared biological processes for validated targets of miR-103a-3p and miR-378a-5p.

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