**SUPPLEMENTARY FIGURE LEGENDS**

**Figure S1.**

Characteristics of chemoresistant prostate cancer cells. **A**, Table summarizing the androgen receptor status and the maximum resistance dose obtained with docetaxel and cabazitaxel for IGR-CaP, PC3, LNCaP and 22RV1. **B**, Clonogenicity assay; pictures of the representative stained clones obtained for parental or chemoresistant cells after control, docetaxel or cabazitaxel administration. Colony count is represented as mean ±SD.

**Figure S2.**

**A**, Upregulation of FKBP7 mRNA levels in chemoresistant prostate cancer cells.Quantitative RT-PCR (qRT-PCR) of FKBP7 mRNA level in docetaxel (Dtx-R) or cabazitaxel (Cbx-R) resistant cells, normalized to parental cells and GUSB. Data shows mean ±SD (n=3). **B**, Increase in FKBP7 expression with microtubule-targeting agents. Immunoblot showing FKBP7 and HSPA5/BiP protein levels in various parental cells after treatment with 100nM nocodazole or 5nM paclitaxel for 24h, 48h and 120h. Actin was the loading control.

**Figure S3.**

Effect of FKBP7 silencing and FKBP7 overexpression on cell proliferation and taxane response. **A,** Cell viability was determined daily (WST1 assay) after transfection with siRNA (targeting FKBP7 or control siNT) in parental cell (solid line) or in resistant cells (dotted line). Cell proliferation levels were normalized to siNT condition respectively. Data are presented as mean ±SD (n=3). \*p<0.005; \*\*p<0.001; \*\*\*p<0.0005; \*\*\*\*p<0.0001 as determined by two-way ANOVA with Bonferroni posttests. **B,** Cell viability was determined daily in siRNA-transfected chemoresistant cells 1, 2 or 3 days after treatment with docetaxel (arrow) at their respective maximum resistance dose (solid line) or without treatment (dotted line). Cell proliferation levels were normalized to siNT condition respectively. Data are presented as mean ±SD (n=3). Two-way ANOVA with Bonferroni modification was performed. **C,** Immunoblot shows FKBP7 overexpression after transduction of parental IGR-CaP1 and 22RV1 cells with lentivirus expressing FKBP7 *versus* control vector. Cell viability of lenti-Ctrl (●) or lenti-FKBP7 (○) expressing cells was assessed after 72h of treatment with increasing concentrations of docetaxel or paclitaxel. Data are presented as mean ±SD. IC50 values were determined with Graphpad software.

**Figure S4.**

**A,** Increase of the tumorigenicity of chemoresistant tumors through successive passages in mice.Tumor growth during the five passages generated the docetaxel resistant mouse model. The data shows the mean ±SEM. **B,** Proliferation assay. Cell viability (*versus* control treatment) of docetaxel-resistant IGR-CaP1-Rvivo cells transduced with lentivirus expressing two shRNAs targeting FKBP7 (sh-a and sh-b) *versus* control shRNA, after 120h of treatment with increasing doses of docetaxel. Data are presented as mean ±SD.

**Figure S5.**

FKBP7 silencing does not affect cell growth in non-tumorous cells. **A**, Immunoblot showing FKBP7 protein level in various non-cancerous cells, with IGR-CaP1-Dtx-R as a control of FKBP7 expression. Actin was the loading control. Quantification of FKBP7/actin was performed (Image Lab software). **B**, Immunoblot shows FKBP7 knockdown efficiency 48h after transfection with either one of two different siRNA sequences targeting FKBP7 [siFK-1 (●) or siFK-2 (○)] or control siRNA (siNT, ■). Cell viability in cells transfected with either one of two different siRNA sequences targeting FKBP7, or control siRNA was determined daily with WST1.

**Figure S6.**

FKBP7 regulates the activity of eIF4F translation initiation complex through a direct interaction with eiF4G. **A**, Overexpressed FKBP7 was immunoprecipitated with anti-FKBP7 antibody (or IgG as control) in IGR-CaP1 and 22RV1 cells transduced with lenti-FKBP7 vector. Immunoblot showing eIF4G and HSPA5/BiP, but not eIF4A as co-immunoprecipited proteins. Input controls (20%) are shown. Star showing bands corresponding to Ig. **B**, Total protein synthesis is affected by FKBP7 silencing in parental IGR-CaP1 cells. Total AHA incorporation is examined by immunoblot. Total protein synthesis labeled by biotinylated AHA was detected by streptavidin-conjugated HRP-labeled antibody and chemi-luminescence. The total signal was quantified by ImageLab. The eIF4G and FKBP7 levels were controlled by immunoblot. **C**, Quantitative RT-PCR of eIF4G mRNA and FKBP7 mRNA in Dtx-R and Cbx-R IGR-CaP1 and 22RV1 cells transfected with siNT, siFK-1 or siFK-2. The eIF4G and FKBP7 levels were normalized to siNT condition. Data represent mean ±SEM. *P value* was obtained using the two-tailed Student’s t test. (\*\*p <0.001 ; \*\*\*p <0.0005 ; \*\*\*\*p <0.0001). **D,** Proximity ligation assay (PLA) performed in order to prove the specificity of FKBP7-eIF4G interaction. The interactions studied are noted in grey rectangles and the probes used are listed. The expression of FKBP7 and of eIF4G, and the interaction FKBP7-eIF4G were detected in docetaxel-resistant IGR-CaP1 and 22RV1. The interactions were visualized as red dots and the nuclei are in blue. The white numbers indicate the mean calculated on at least 100 cells. Bars represent 20µm. **E,** PLA was performed 48h after transfection of IGR-CaP1-Dtx-R with 10nM siRNA targeting eIF4G (si4G) or control siRNA (siNT). The expression of eIF4G and the interactions FKBP7-eIF4G and eIF4G-eIF4E were detected and counted (n>6000 cells). Data (mean ±SD) were normalized to siNT in 4G condition. *P value* was obtained using the two-tailed Student’s t test (\*\*\*\*p <0.0001). The effect of eIF4G silencing on the number of dots/cell is indicated by the ratio siNT/si4G.

**Figure S7.**

**A,** Expression of MDR1 in prostate cancer cell lines**.** Immunoblots show MDR1 level in parental (S) and docetaxel (Dtx) or cabazitaxel (Cbx) resistant IGR-CaP1, PC3, LNCaP and 22RV1. Actin was the loading control. **B,** The effect of the combination of docetaxel with flavaglines on cell proliferation of chemoresistant cells**.** Cell viability (calculated relatively to control treatment) of docetaxel-resistant cells IGR-CaP1 and 22RV1 treated either with flavagline 3 or 23 alone (dotted line) or in association with 50nM docetaxel 50nM (solid line) for 72h. The data are represented as the mean ±SEM. **C,** IC50 determination in parental (S) and docetaxel resistant IGR-CaP1 and 22RV1 or in melanoma A375 treated with FL3 or FL3, alone or in combination with 50nM Docetaxel for 72h. IC50 values were estimated with a weighted 5-parameter logistic regression using GraphPad software. **D**, Mechanistic model of the role of FKBP7 in prostate cancer cells. By directly binding to eIF4G, overexpression of FKBP7 in chemoresistant cells leads to increased translational activity of eIF4F, and thus to the survival of chemoresistant cancer cells. Inhibitors of this pathway are indicated. Only the flavaglines (FL3 and FL23) efficiently inhibited this pathway, leading to cell death of the chemoresistant cells.