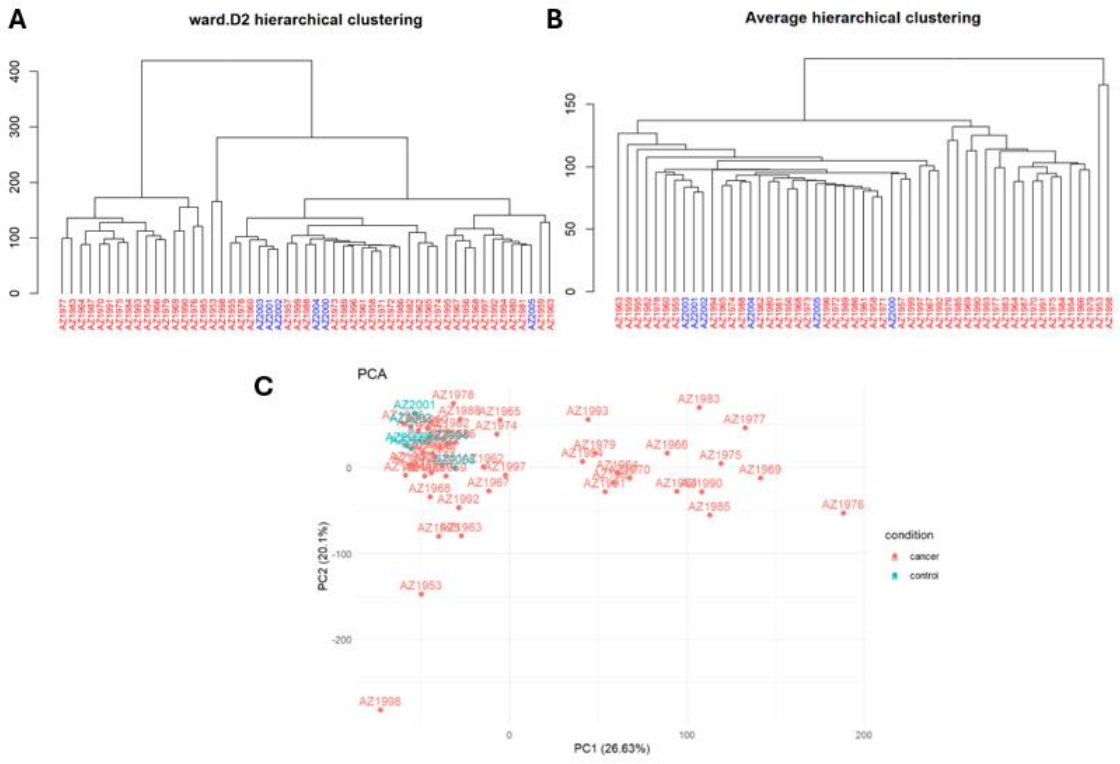
SUPPLEMENTARY MATERIALS

Supplementary Figure 1

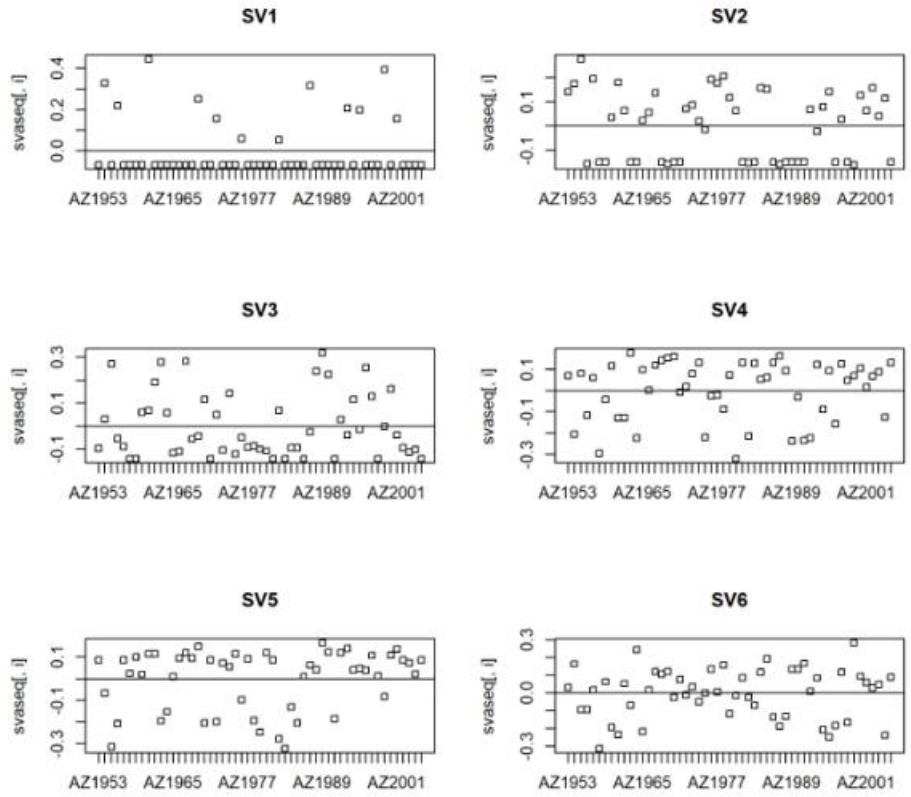
Supplementary Figure 1: Sequence quality histogram. It is displaying the mean quality value across each base position in the read. All bases are located within the green fragment.

Supplementary Figure 2



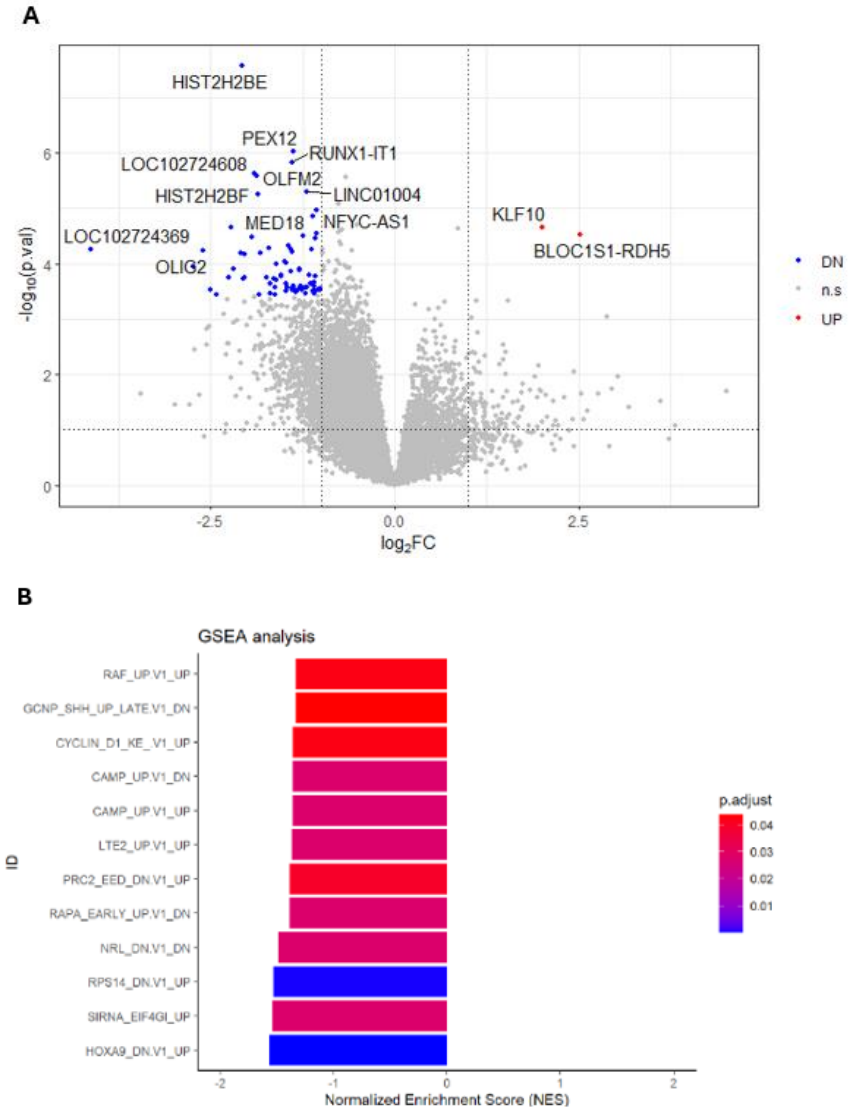
Supplementary Figure 2: Clustering methods. (A, B) Hierarchical clustering of the samples, considering all genes, using the Euclidean distance and Ward.D2 (A) and average (B) linkage methods. (C) PCA plot representing the first two principal components. In the three plots, control cases are coloured in blue and cancer cases in red. PCA: Principal Component Analysis, PC1: Principal Component 1, PC1: Principal Component 2.

Supplementary Figure 3



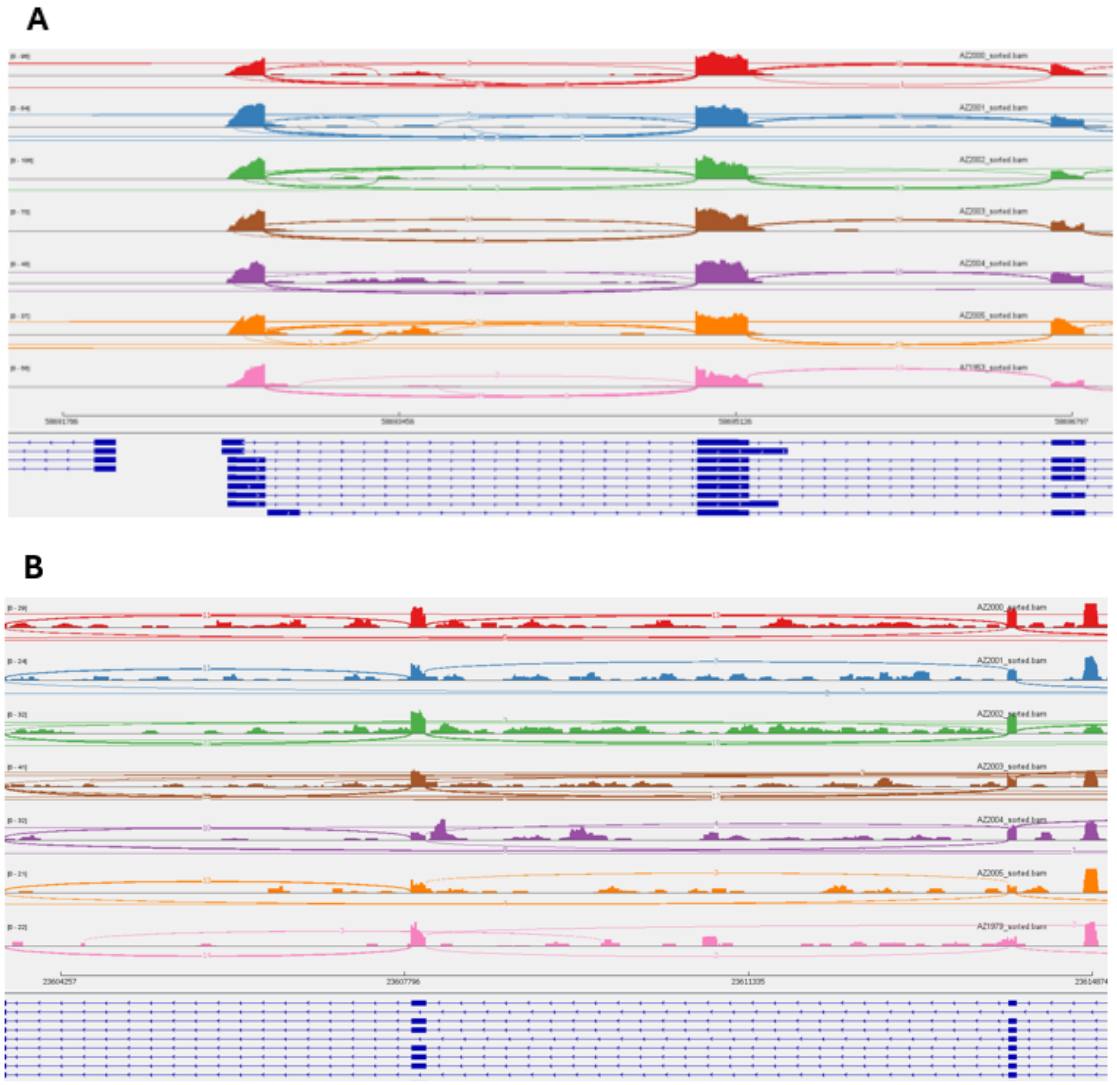
Supplementary Figure 3: Surrogate variables. Surrogate variables found in the data when considering the different samples. SV: Surrogate Variable.

Supplementary Figure 4



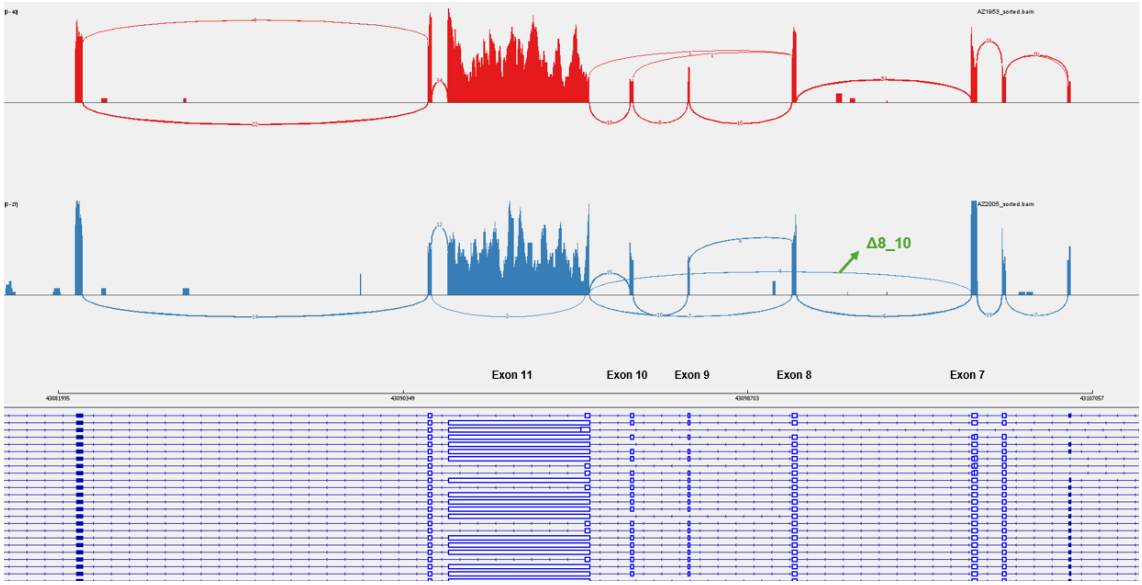
Supplementary Figure 4: Differentially expressed genes and oncogenic signature analysis. (A) Volcano plot showing the DEGs (adjusted p-value < 0.05 and |logFC| > 1) after comparing the 47 cancer samples against the 6 control samples. Down-regulated genes are coloured in blue, not-significant are coloured in grey and up-regulates are coloured in red. (B) Gene set enrichment analysis (GSEA) selecting the C6 oncogenic signature gene sets from MSigDB. The adjusted p-value for each associated set is represented using a colour scale. FC: Fold-change, DN: Down-regulated, n.s: not-significant, UP: Up-regulated, GSEA: Gene Set Enrichment Analysis.

Supplementary Figure 5



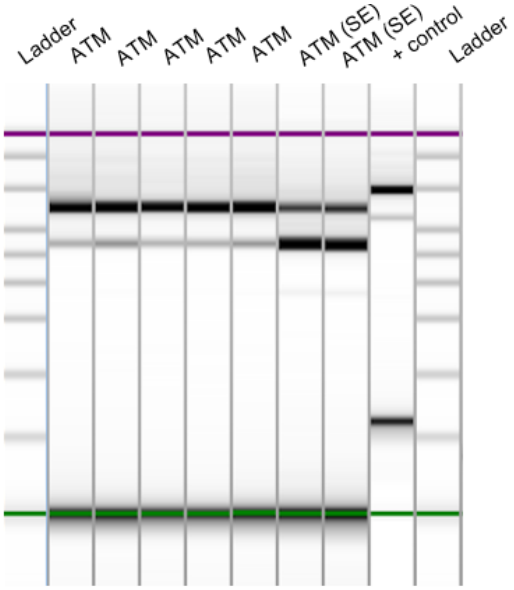
Supplementary Figure 5: IGV visualization and Sashimi plots of alternative splicing events. (A) Visualization of an AF local event present in the cancer sample AZ1953 (pink) and absent in all other control samples. (B) Visualization of a SE local event present in the cancer sample AZ1979 (pink) and absent in all other control samples.

Supplementary Figure 6



Supplementary Figure 6: IGV visualization and Sashimi plot of alternative splicing events. Visualization of the deletion in exons 8 to 10 (Δ8_10) is shown for the cancer sample AZ1953 (red) and the control sample AZ2005 (blue).

Supplementary Figure 7



Supplementary Table 7: **ATM splicing event validation:** Electrophoresis gel showing the full length of the *ATM* gene (upper band) in all lanes except the ladders. Additionally, in the lanes labelled ATM (SE), a lower band corresponding to an exon skipping event for exon 9 of the *ATM* gene can be observed, which validates the results obtained from the FRASER analysis for the AZ1954 sample. A positive control (+ control) for the *ATM* exon skipping event is also included. SE: Exon skipping.

Supplementary Table 1

Supplementary Table 1: **Percentage of duplications.** Table indicating the percentage of duplications observed in each of the samples analyzed.

Supplementary Table 1: Number of counts and percentage of duplications

Sample ID	Counts number (millions)	% of duplications
AZ1953	95	39.4
AZ1954	79	31.5
AZ1955	74.7	33.2
AZ1956	103.4	35
AZ1957	77.3	31.6
AZ1958	195.1	38.1
AZ1959	207.2	39.7
AZ1960	167.7	35.3
AZ1961	179.1	35.7
AZ1962	159	36.8
AZ1963	73.1	25
AZ1964	166.9	35.2
AZ1965	221.9	38.5
AZ1966	130.4	32.2
AZ1967	120	32.3
AZ1968	98.2	33.7
AZ1969	78.3	46.2
AZ1970	87.4	31.2
AZ1971	90.6	32.1
AZ1972	85.3	30.5
AZ1973	82.4	32.1
AZ1974	108.6	29.3
AZ1975	103.2	33
AZ1976	78.4	32.7
AZ1977	74.4	30.5
AZ1978	67.6	27.8
AZ1979	73.5	27.4
AZ1980	98.2	29
AZ1981	70.3	28.3
AZ1982	122.1	34.9
AZ1983	125.2	29.8
AZ1984	108.3	33.3
AZ1985	82.5	31.8
AZ1986	88.4	27
AZ1987	116.2	30.5
AZ1988	72.5	27.4
AZ1989	75.1	28.6
AZ1990	116.5	34.4
AZ1991	114.1	32.3
AZ1992	93	28.6
AZ1993	82.6	28.3
AZ1994	72.7	27.9
AZ1995	80.1	31.2
AZ1996	91.8	29.4
AZ1997	71.4	26.4
AZ1998	109.2	34.4
AZ1999	100.8	32.5
AZ2000	102.9	30.2
AZ2001	83.7	30.2
AZ2002	121.6	31.3
AZ2003	106.5	31.1
AZ2004	82.4	26.7
AZ2005	94.6	28.3

Supplementary Table 2

***Supplementary Table 2:* Patient data.** Table indicating the family, code, sex and cancer type of each patient included in the study.

Supplementary Table 2: Patient data			
Family	**Code**	**Sex**	**Cancer type**
d11q	AZ1970	F	Healthy
CM-1	AZ1971	F	BC
CM-2	AZ1954	F	BC
CM-3	AZ1986	F	OC
CM-3	AZ1987	F	BC
CM-4	AZ1953	F	BC
CM-5	AZ1976	F	BC
CM-6	AZ1981	F	BC
CM-7	AZ1963	F	BC, OC and Triple-negative breast cancer
CM-8	AZ1995	F	BC
CM-9	AZ1957	F	BC
CM-10	AZ1955	F	BC
CM-11	AZ1982	F	BC
CM-12	AZ1968	F	BC
CM-13	AZ1956	F	OC
CM-13	AZ1967	F	BC
CM-14	AZ1978	F	BC
CM-15	AZ1958	F	BC
CM-16	AZ1964	F	BC, OC
CM-17	AZ1974	F	BC
CM-18	AZ1959	F	BC
CM-19	AZ1989	F	BC
CM-20	AZ1960	F	BC
CM-21	AZ1969	M	BC
CM-22	AZ1975	F	BC, Bone, Colorectal
CM-23	AZ1961	F	BC
CM-24	AZ1965	F	BC and OC
CM-25	AZ1962	F	BC / Endometrium
CM-26	AZ1999	F	OC
CM-27	AZ1983	F	BC
CM-28	AZ1966	F	BC
CM-29	AZ1972	M	BC
CM-30	AZ1973	F	BC, Melanoma
CM-31	AZ1977	F	BC
CM-32	AZ1979	F	BC
CM-33	AZ1980	F	BC
CM-34	AZ1984	F	BC
CM-35	AZ1985	F	BC
CM-36	AZ1988	F	BC

CM-37	AZ1990	F	BC
CM-38	AZ1991	F	Melanoma
CM-39	AZ1996	F	Pancreas adenocarcinoma
CM-40	AZ1993	F	BC
CM-41	AZ1994	F	BC
CM-42	AZ1998	F	OC
CM-43	AZ1997	M	BC
PANC-44	AZ1992	M	Pancreas adenocarcinoma
control sa	AZ2000	M	Healthy
control sa	AZ2001	F	Healthy
control sa	AZ2002	F	Healthy
control sa	AZ2003	F	Healthy
control sa	AZ2004	F	Healthy
control sa	AZ2005	F	Healthy