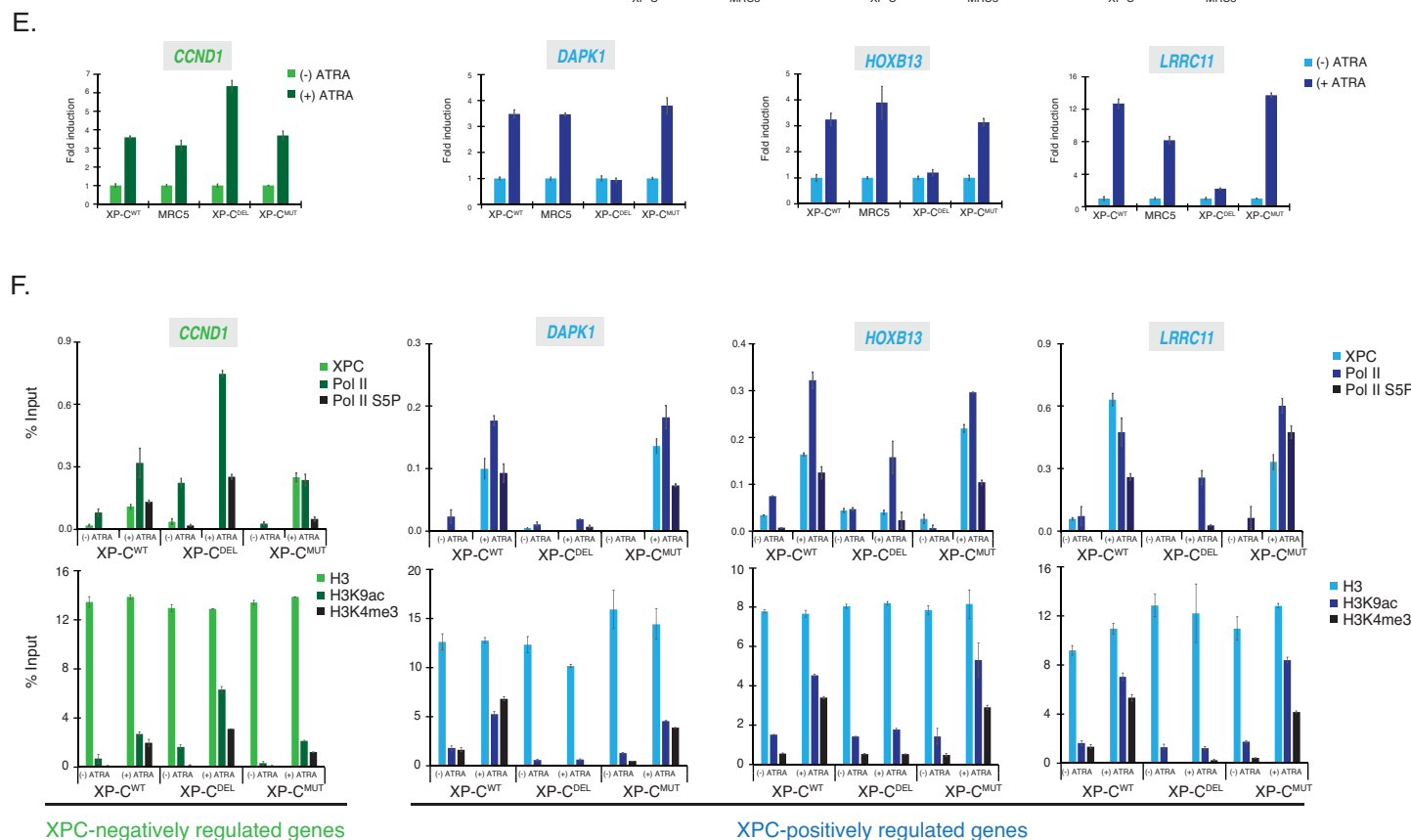
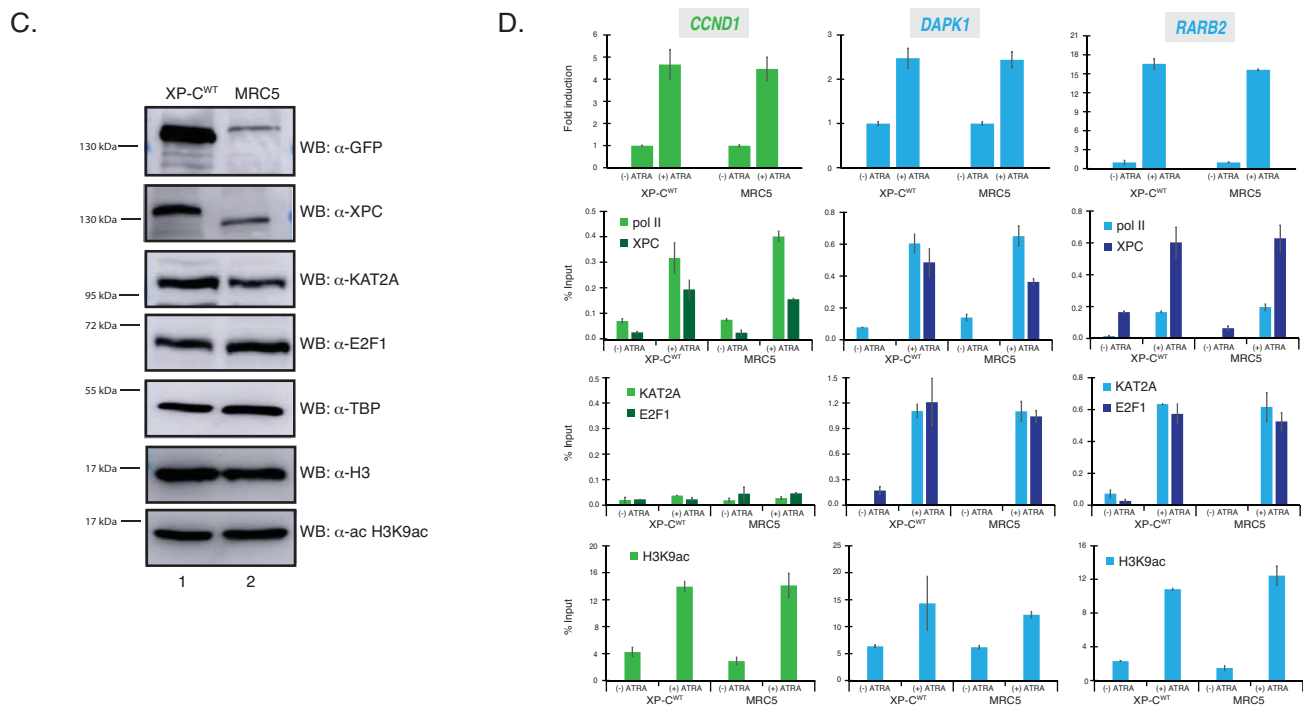
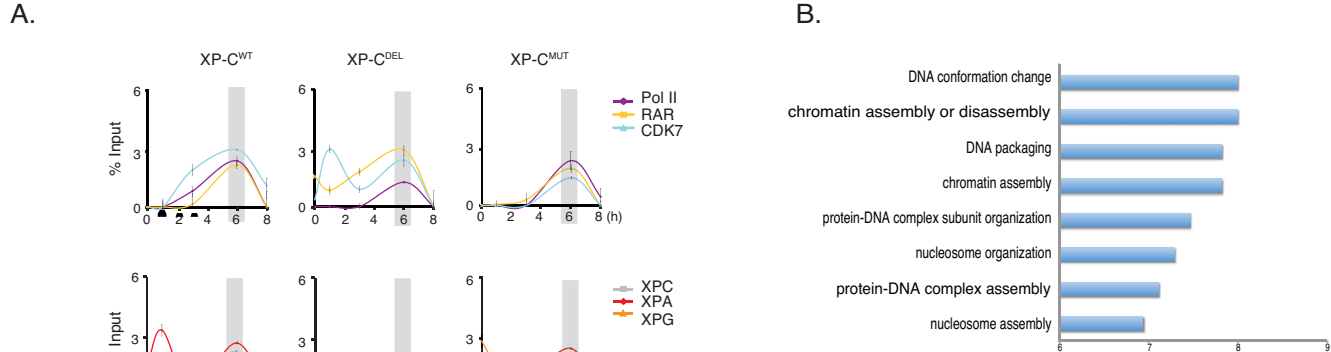


Supplementary Methods

Microarray analysis

Total RNA from shXPC, XP-CDEL and shCtrl cells were extracted before or 6 hours after t-RA treatment (10 μ M) using GenElute Mammalian Total RNA Miniprep kit (Sigma). Two independent experiments were performed. RNA quality was verified by analysis on the 2100Bioanalyzer (Agilent). Biotinylated single strand cDNA targets were prepared, starting from 250 ng of total RNA, using the Ambion WT Expression Kit (Cat # 4411974) and the Affymetrix GeneChip® WT Terminal Labeling Kit (Cat # 900671), according to Affymetrix recommendations. Following fragmentation and end-labeling, 1.9 μ g of cDNAs were hybridized for 16 hours at 45°C on GeneChip® Human Gene 1.0 ST arrays (Affymetrix) interrogating 28,853 genes represented by approximately 27 probes spread across the full length of the gene. The chips were washed and stained in the GeneChip® Fluidics Station 450 (Affymetrix) and scanned with the GeneChip® Scanner 3000 7G (Affymetrix). Finally, raw data (CEL Intensity files) were extracted from the scanned images using the Affymetrix GeneChip® Command Console (AGCC) version 3.1. CEL files were further processed with Affymetrix Expression Console software version 1.1 to calculate probeset signal intensities using Robust Multi-array Average (RMA) algorithms with default settings.



Supplementary Figure 1: NER factors, transcriptional machinery and histone PTMs at XPC target-genes and their gene-ontology annotations.

A-ChIP experiments monitoring the occupancy of Pol II, RAR, CDK7, XPC, XPA and XPG at *RARβ2* promoter for up to 8 hours in chromatin extracts from XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells. Error Bars represent the standard deviation of three independent experiments.

B-Gene ontology annotation performed with DAVID 6.7 on XPC-positively regulated genes.

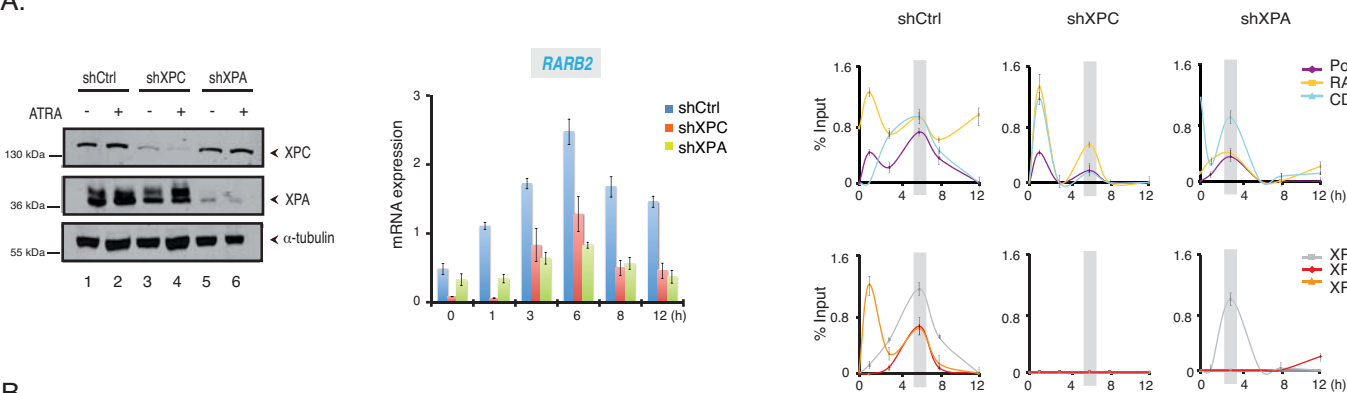
C- Relative protein expression of XPC, GFP-XPC, KAT2A, E2F1, TBP, H3 and H3K9ac analysed by Western Blot from whole cell and nuclear extracts from XP-C^{WT} and MRC5 cells.

D- Fold induction of *RARβ2*, *DAPK1* and *CCND1* in XP-C^{WT} and MRC5 fibroblasts, after ATRA treatment during 6 hours (upper panels). Occupancy of XPC, Pol II, KAT2A, E2F1 (central panels) and H3K9ac (lower panels) at promoters of XPC- negatively regulated gene *CCND1* and XPC-positively regulated genes *DAPK1* and *RARβ2*, monitored by ChIP from chromatin extracts of XP-C^{WT} and MRC-5 cells in presence or absence of ATRA. All the Error Bars represent the standard deviation of three independent experiments.

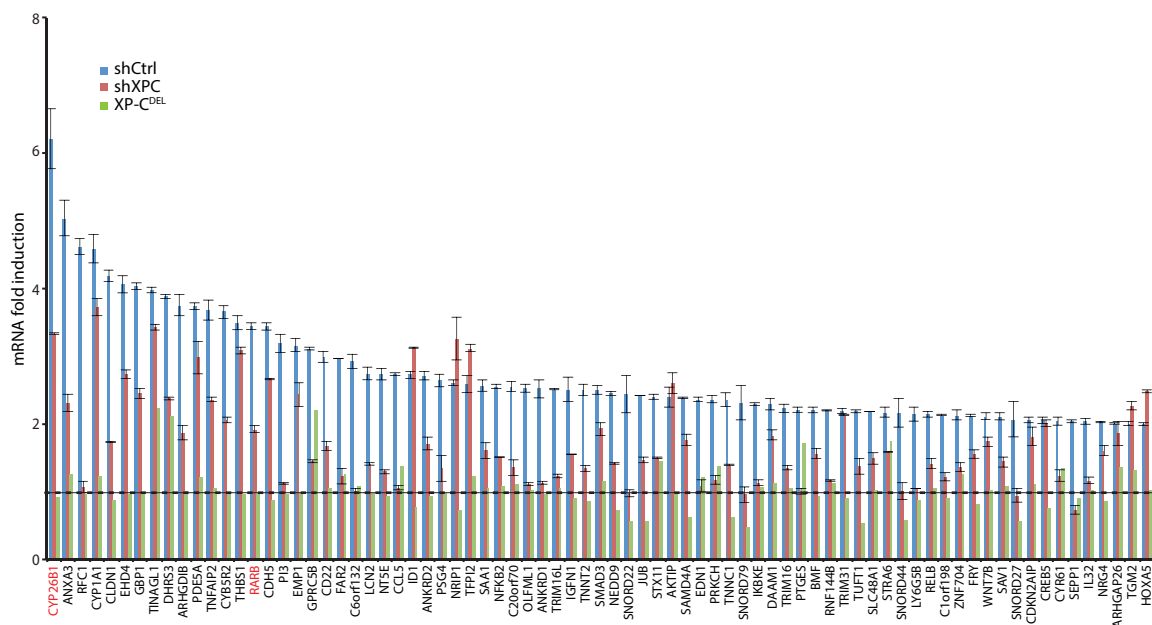
E- Fold induction of XPC-positively regulated *DAPK1*, *HOXB13*, *LRCC11* and XPC-negatively regulated *CCND1* in XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} and MRC5 fibroblasts, after ATRA treatment during 6 hours. Error Bars represent the standard deviation of three independent experiments.

F- Occupancy of XPC, Pol II and Serine 5 phosphorylated Pol II (Pol II S5P) (Upper panel) or H3, H3K9ac and H3K4me3 (lower panel) at promoters of XPC-negatively regulated gene *CCND1* and XPC- positively regulated genes *DAPK1*, *HOXB13* and *LRRC11*, monitored by ChIP from chromatin extracts of XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells in presence or absence of ATRA. Error Bars represent the standard deviation of three independent experiments.

A.



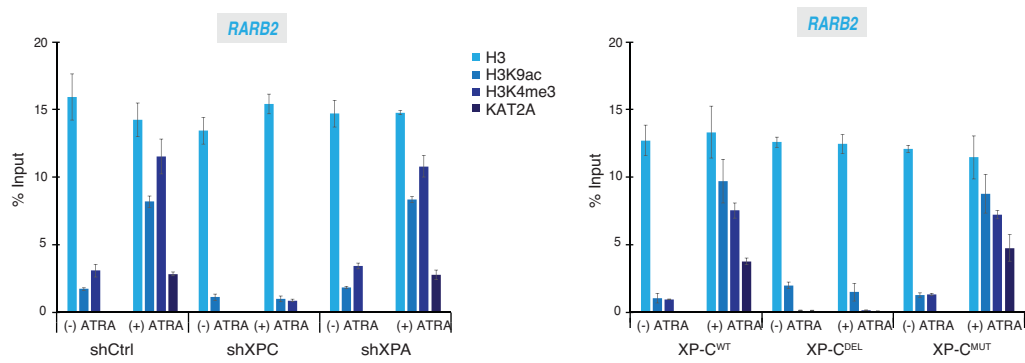
B.



C.



D.



Supplementary Figure 2: Characterization of active Histone PTMs marks H3K9ac and H3K4me3 in XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells and characterization of shCtrl, shXPC and shXPA cells for NER factors and transcriptional machinery.

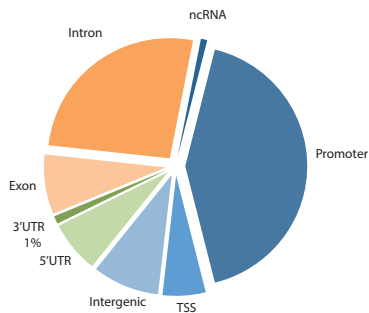
A- Relative protein expression of XPC and XPA analysed by Western Blot from whole cell extract from shCtrl, shXPC or shXPA HeLa cells, in presence or absence of ATRA (left panel). Relative mRNA expression of *RARβ2* in shCtrl, shXPC or shXPA HeLa cells after ATRA treatment in 12 hours' time course experiment (central panel). Corresponding recruitment of Pol II, RAR, CDK7, XPC, XPA and XPG at *RARβ2* promoter for up to 12 hours as monitored by ChIP (right panel). Error bars represent the standard deviation of three independent experiments.

B- Transcriptome profiling of shCtrl (blue), shXPC (red) and XP-C^{DEL} (green) cells treated with ATRA during 6 hours using the whole transcript coverage Affymetrix Human Gene 1.0 ST arrays. Based on two independent experiments, these genes show an up-regulation > to 2 (±SEM) compared to t=0 hour (F-test, P<0.005).

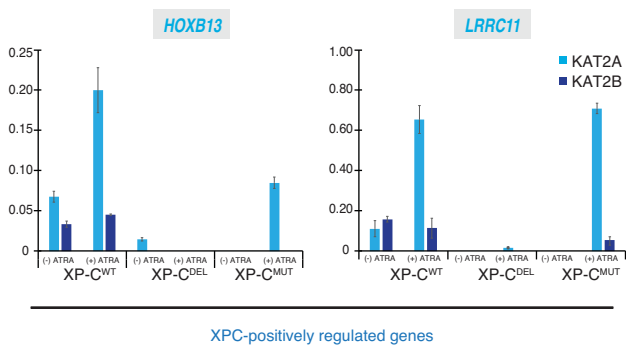
C- Protein expression of KAT2A and TBP analysed by Western Blot from whole cell extracts from shCtrl, shXPC or shXPA HeLa cells (left panel) and from XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} fibroblasts (right panel), in presence or absence of ATRA.

D- ChIP experiment monitoring for recruitment of KAT2A and deposition of Histone H3, H3K9ac, H3K4me3 at *RARβ2* promoter using chromatin extracts from shCtrl, shXPC or shXPA HeLa cells (left panel) and XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} fibroblasts (right panel), in presence or absence of ATRA. Error bars represent the standard deviation of three independent experiments.

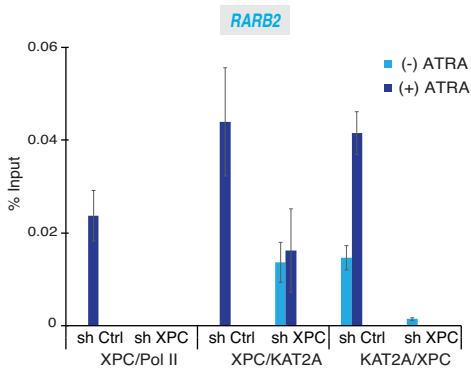
A.



B.



C.



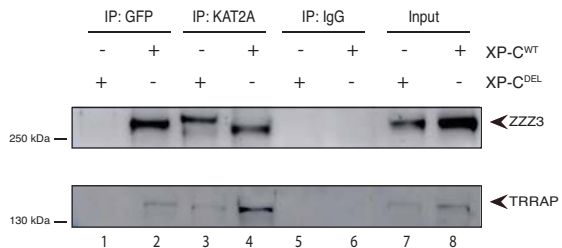
Supplementary Figure 3: KAT2A is recruited XPC-positively regulated genes

A- HOMER annotation of KAT2A.

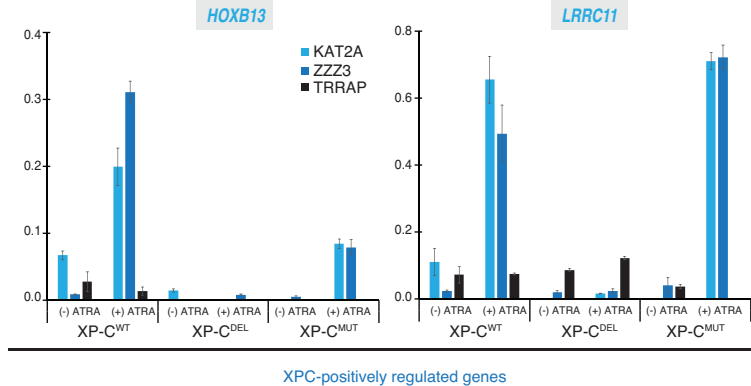
B- ChIP experiments monitoring the occupancy of KAT2A and KAT2B at promoters of XPC-positively regulated genes *HOXB13* and *LRRC11* from chromatin extracts of XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells in presence or absence of ATRA. Error bars represent the standard deviation of three independent experiments.

C- ChIP/Re-ChIP experiment monitoring the co-occupancy of either XPC and Pol II or XPC and KAT2A in shCtrl and shXPC HeLa cells at *RARβ2* promoter upon ATRA treatment. Error bars represent the standard deviation of three independent experiments.

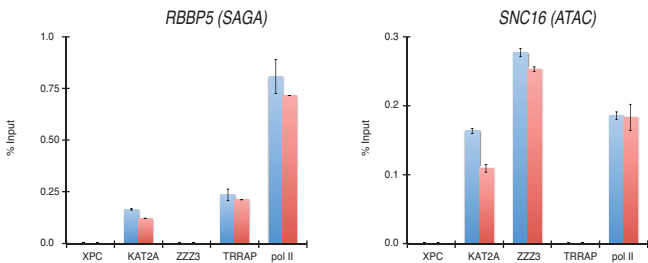
A.



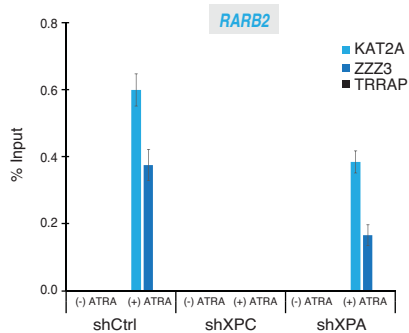
B.



C.



D.



Supplementary Figure 4: XPC is found in both ATAC and SAGA complexes but only ATAC was detected at XPC-target promoters upon transcription.

A- Immunoprecipitation performed on nuclear extracts from XP-C^{WT} or XP-C^{DEL} fibroblasts with antibody against GFP, KAT2A or IgG. Western Blot was revealed with antibodies directed against ZZZ3 (ATAC) and TRRAP (SAGA).

B- ChIP experiment investigating the occupancy of KAT2A, ZZZ3 and TRRAP at promoters of XPC-positively regulated genes *HOXB13* and *LRRC11* from chromatin extracts of XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells in presence or absence of ATRA. Error bars represent the standard deviation of three independent experiments.

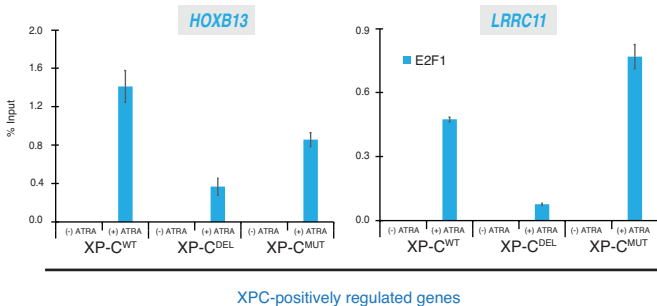
C- ChIP experiment monitoring the occupancy of XPC, KAT2A, ZZZ3, TRRAP and Pol II at *RBBP5* (targeted by SAGA) and *SNC16* (targeted by ATAC) promoters using chromatin extracts from XP-C^{WT} and XP-C^{DEL} fibroblasts. Error bars represent the standard deviation of three independent experiments.

D- ChIP experiment analysing the recruitment of KAT2A, ZZZ3 and TRRAP at *RARβ2* promoter using chromatin extracts from shCtrl, shXPC or shXPA HeLa cells, before and after ATRA treatment. Error bars represent the standard deviation of three independent experiments.

A.

	Raw P-Value	Hyper FDR Q-Val	Total Genes
Motif TTTCSCGC matches E2F1: E2F transcription factor 1	1.991889e-12	3.300984825e-9	254/283

B.

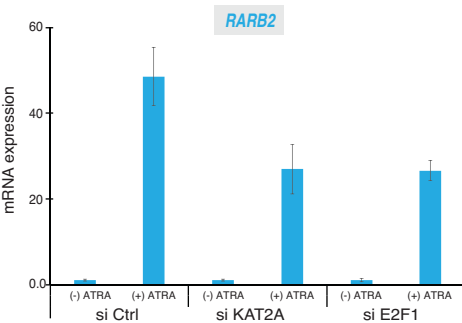


Supplementary Figure 5: XPC-positively regulated genes harbour an E2F1 signature.

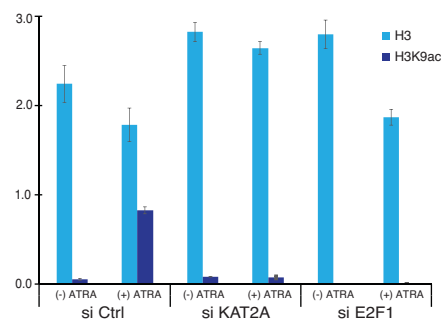
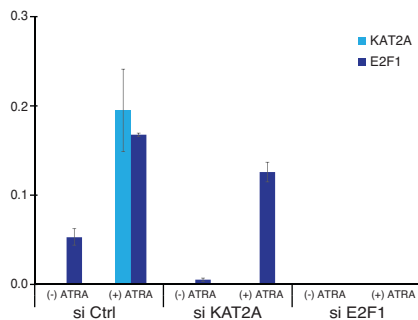
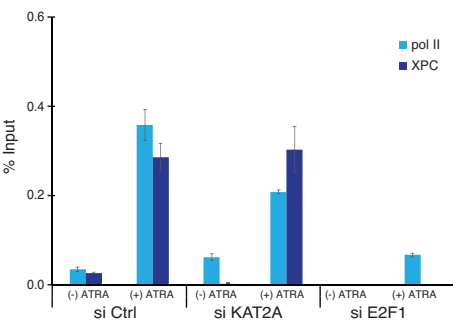
A- Motif research analysis from XPC negatively-regulated and positively-regulated genes promoter sequences using GREAT.

B- ChIP experiment investigating the occupancy of E2F1 at promoters of XPC-positively regulated genes *HOXB13* and *LRRC11* from chromatin extracts of XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} cells in presence or absence of ATRA. Error bars represent the standard deviation of three independent experiments.

A.



B.

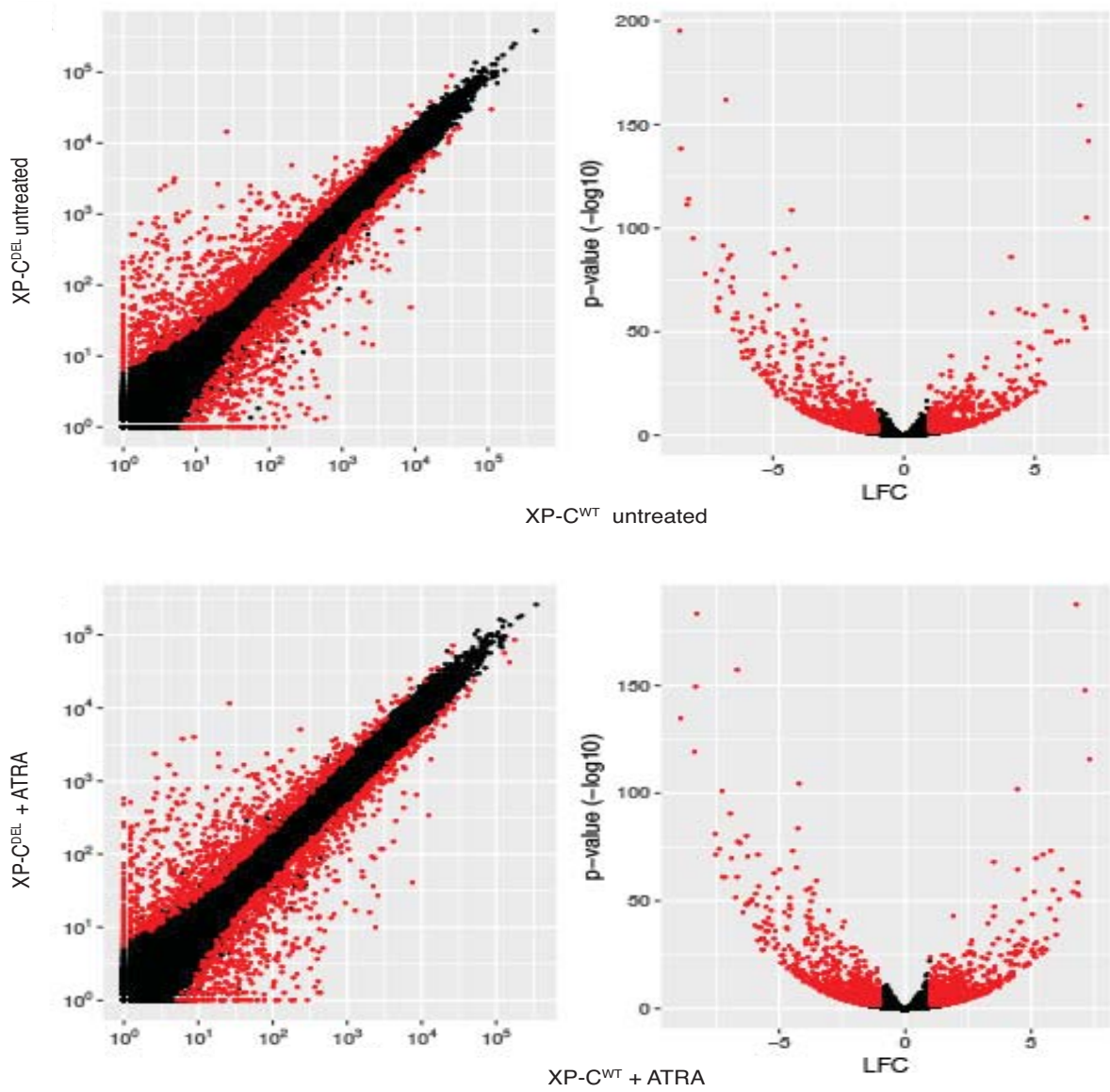


Supplementary Figure 6: XPC and E2F1 are mutually necessary for their recruitment and co-operate to recruit KAT2A at *RARb2* promoter upon transcription.

A- Relative mRNA expression of *RARb2* before and after ATRA treatment in si Ctrl, si KAT2A and si E2F1 XP-C^{WT} cells. Error bars represent the standard deviation of three independent experiments.

B- Corresponding recruitment of Pol II, XPC, KAT2A and E2F1 as well as histone H3 and H3K9ac at *RARb2* promoter monitored by ChIP. Error bars represent the standard deviation of three independent experiments.

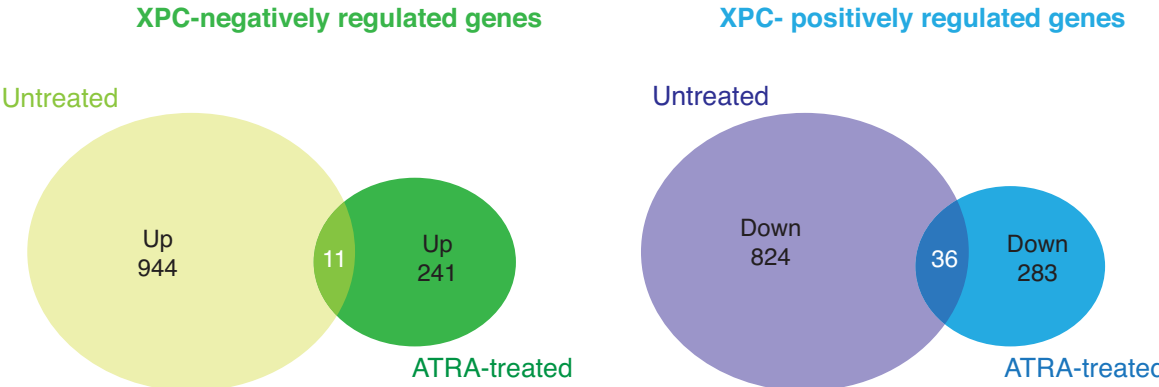
A.



B.

	Over-expressed	Under-expressed	Total
XP-C ^{WT} vs XP-C ^{DEL} untreated	824	944	1,768
XP-C ^{WT} vs XP-C ^{DEL} +ATRA	868	985	1,853

C.



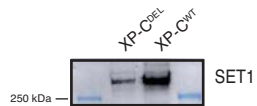
Supplementary Figure 7: XPC regulates positively and negatively subsets of genes in absence or presence of ATRA treatment.

A-Comparison of XP-C^{WT} and XP-C^{DEL} with or without ATRA by RNA-seq. Red points show significant data. All data have been evaluated with DESeq2 R package. Left upper panels and lower panels represent the normalized gene expression without ATRA or after ATRA treatment respectively. For a given gene, its value is obtained by mean on all samples belonging to the same condition plus one. Right upper and lower panels represent the volcano plot for cells without ATRA or after ATRA treatment respectively. The x-axis represents the LFC values and the y-axis the p-values.

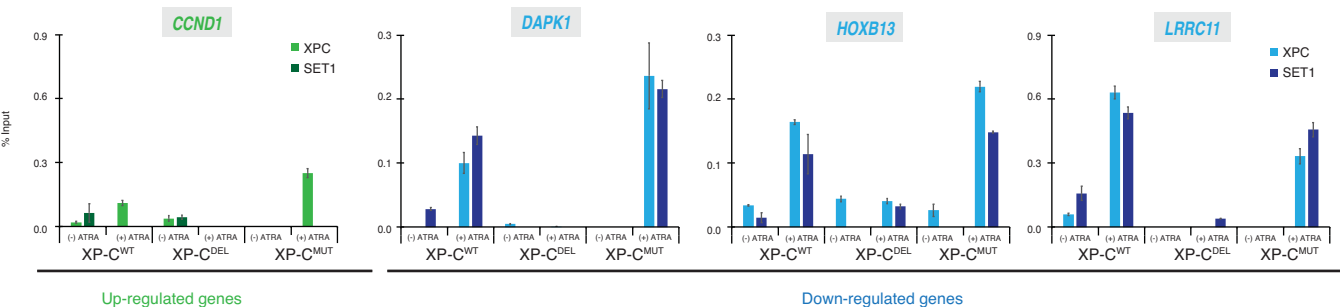
B-Table summarizing the comparative data obtained from the RNA-seq described above between untreated and ATRA-treated XP-C^{WT} and XP-C^{DEL} fibroblasts indicating the numbers of over-expressed and under-expressed genes.

C-Venn Diagram indicating the number of genes commonly either negatively (green) or positively (blue) regulated by XPC in both untreated and ATRA-treated conditions.

A.



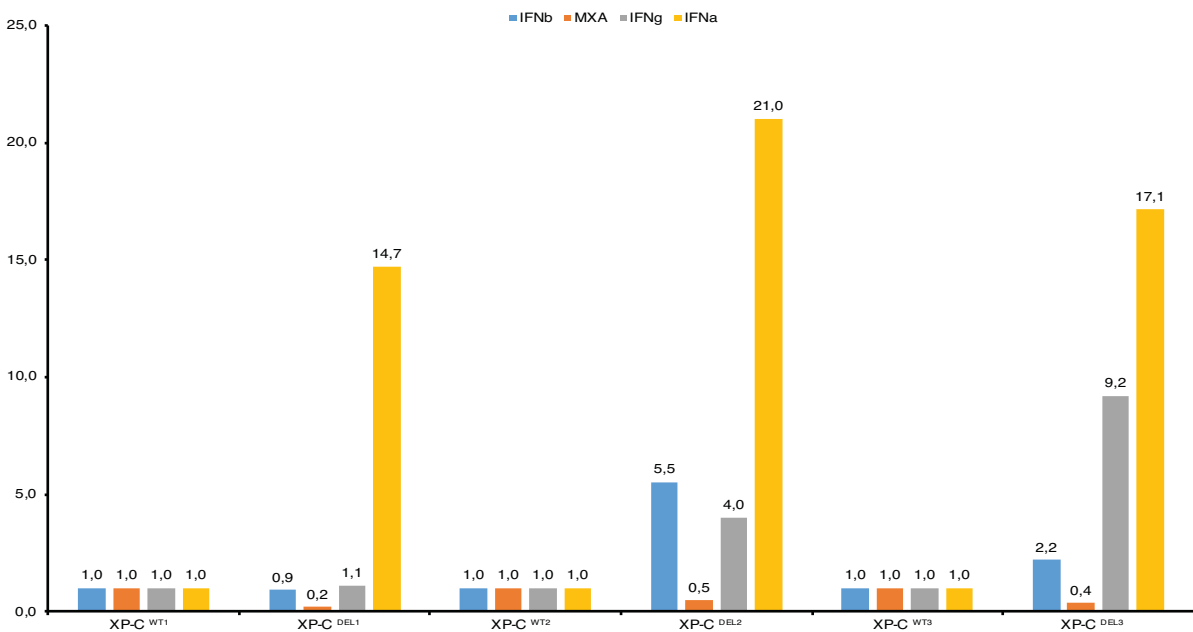
B.



Supplementary Figure 8: XPC directly regulates the expression of SET1 and consequently the deposition of H3K4me3 at XPC-positively regulated promoters.

A- Protein expression of SET1 and TBP analysed by Western Blot from whole cell extract from XP-C^{WT} and XP-C^{DEL} fibroblasts in presence or absence of ATRA.

B- ChIP experiment looking for occupancy of XPC and SET1 at *CCND1*, *DAPK1*, *HOXB13* and *LRRC11* promoters using chromatin extracts from XP-C^{WT}, XP-C^{DEL} and XP-C^{MUT} fibroblasts. Error bars represent the standard deviation of three independent experiments.



Supplementary Figure 9: Untreated Human fibroblasts depleted with XPC highly express IFN compared to XP-C^{WT}.

Relative mRNA expression of *IFN gamma* (*IFNg*), *IFN beta* (*IFNb*), *IFN alpha* (*IFNa*) and *MXA* measured by qRT-PCR in untreated XP-C^{WT} and XP-C^{DEL} fibroblasts.