Supplemental Information

Figure S1.

***P. acnes* infects PrEC cells but has no effect on host cell viability.**

A. Quantification analysis showed that at an MOI of 100 PrEC cells were on average invaded by at least one *P. acnes* cell. Representative results of two independent experiments are shown. *P. acnes*, red; cellular nuclei, blue/cyan. **B.** PrEC cells were infected with *P. acnes* at an MOI of 100 for 24 h with the wild-type strains P6, KPA171202 and 266, as well as the thiopeptide deletion mutant strain. Cell viability was assessed by WST-1 assay.

Figure S2.

Gene interaction network analysis shows cell cycle deregulation in infected cells

A. Pathway analysis of deregulated genes using the DAVID tool revealed that the most significantly enriched KEGG pathway was "Cell cycle" at both 24 h and 48 h p.i. The downregulated genes assigned to cell cycle are highlighted in red. **B.** Interactions between genes deregulated at least 2.5-fold in *P. acnes* P6-infected PrEC cells were depicted with STRING (http://string-db.org/), which visualizes known and predicted protein–protein interactions based on reports within the literature, database entries and/or experimental evidence. Many interacting genes have structural or regulatory roles in kinetochore and centromere assembly and functionality. **C.** Functional analysis of PrEC cell transcriptome responses to *P. acnes* P6 infection at 2 weeks p.i. among genes deregulated at least 2-fold. Similar to short-term infection cell cycle is among the most deregulated networks at 2 weeks p.i.

Figure S3.

Siomycin A treatment inhibits FOXM1

Cells were treated with siomycin A (diluted in DMSO), as a positive control for FOXM1 inhibition, at a concentration of 20 µM for 24 h. Non-infected cells were treated with DMSO. **A.** RT-PCR results of siomycin A treatment for FOXM1 and selected target genes. **B.** Protein expression of FOXM1 is reduced in siomycin A-treated cells to a similar level as in wild-type *P. acnes* (P6)-infected cells

Figure S4.

Effect on FOXM1 by different *P. acnes* strains

P. acnes strains KPA171202 and P6 (both type IB) had the same effect on FOXM1 both on **A.** gene and **B.** protein level. **C.** The effect of the wild-type strain on FOXM1 required the presence of live *P. acnes* since heat-killed (HI) bacteria did not alter FOXM1 expression. *P. acnes* 266 (type IA) that does not contain the thiopeptide encoding gene cluster, had only a moderate effect on FOXM1 expression. To exclude the effects of tetracycline (TCN) on FOXM1 expression, non-infected cells were treated with 50 µg/ml tetracycline for 24 h (NI + TCN).

Supplementary Table 1. Significantly differentially expressed genes between *P. acnes* P6 infected and non-infected PrEC cells at 24 h, 48 h and 2 weeks post-infection.

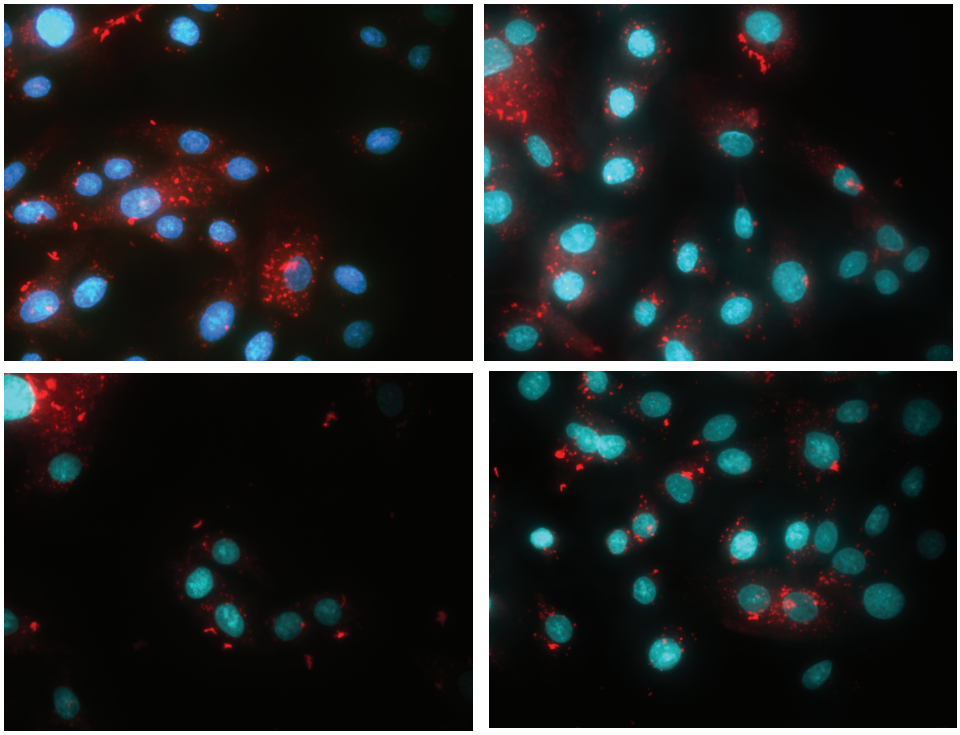
Supplementary Table 2. List of all primers used in this study.

Supplementary Table 3. Quantification of intracellular bacteria in PrEC cells

An antibiotic protection assay was carried out. PrEC cells were infected with different strains of P. acnes at an MOI of 100. Extracellular cells were killed at 24 h p.i. and intracellular bacteria were determined by colony forming unit (CFU) counts. The thiopeptide mutant strain was efficiently invading PrEC cells, at a slightly higher frequency than the wild-type strain. HI: heat-inactivated.

Supplementary Figure 1

A



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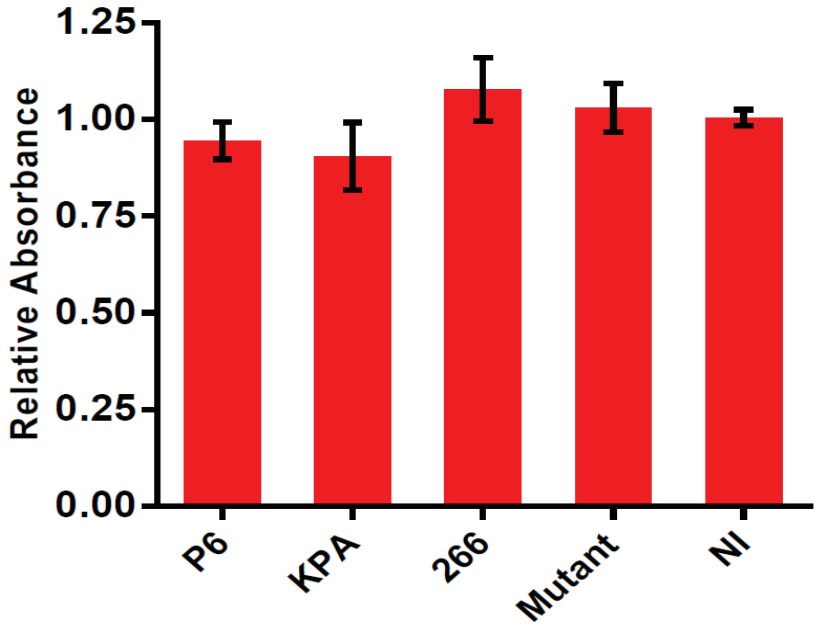
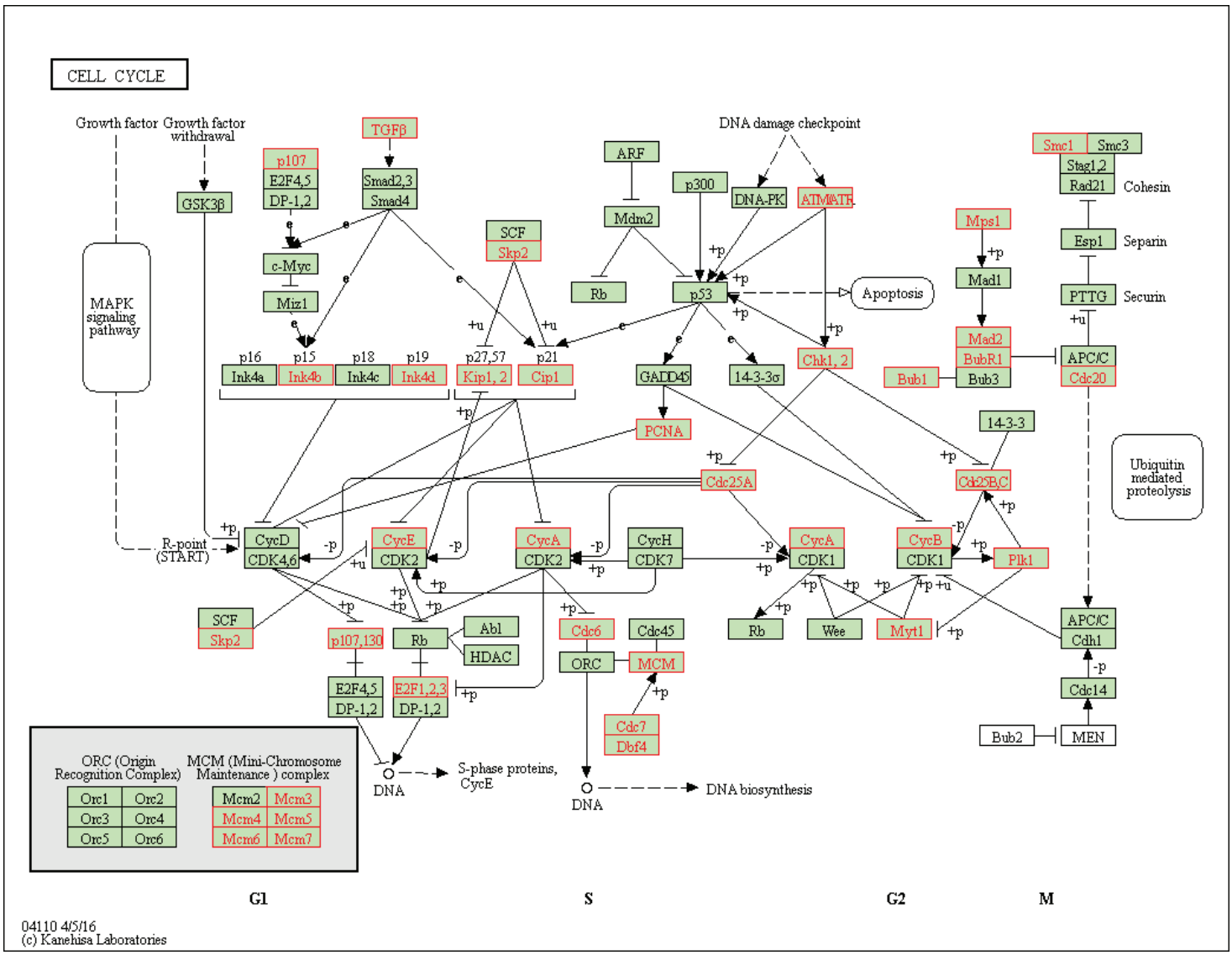


Supplementary Figure 2

A



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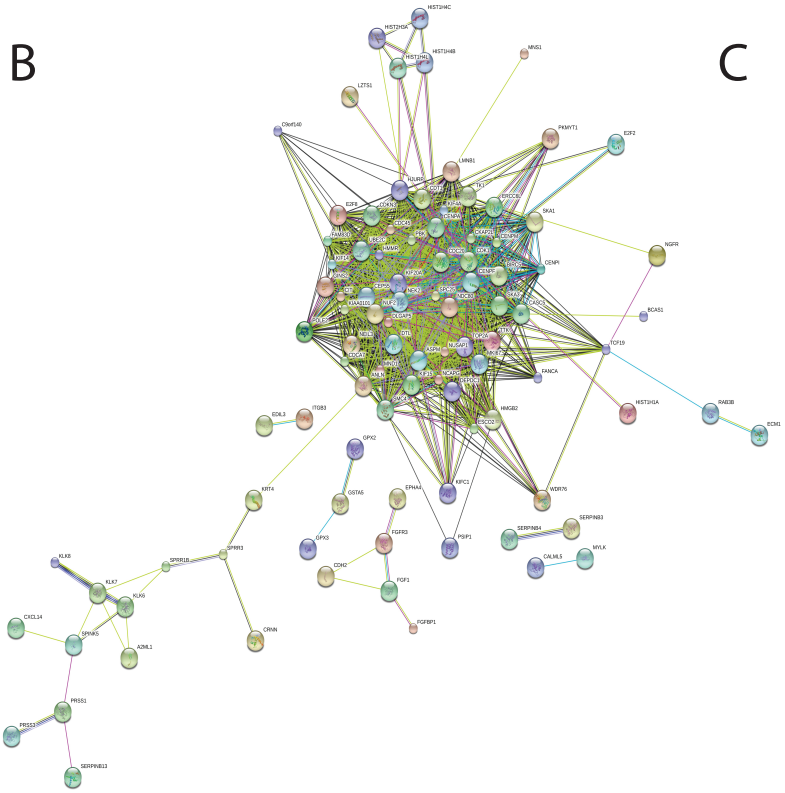

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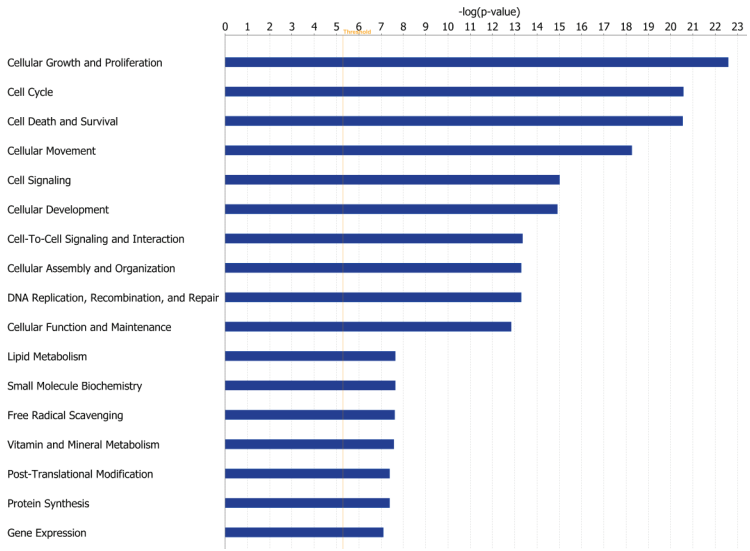
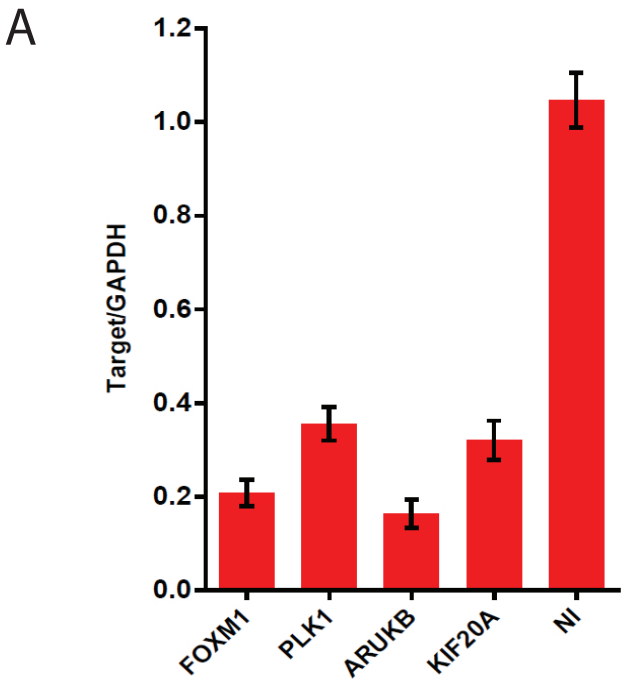
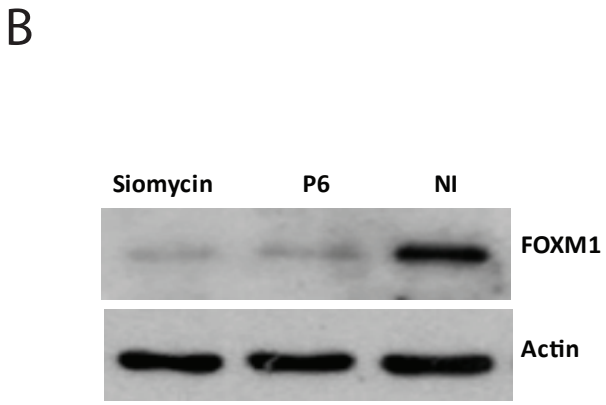


Supplementary Figure 3





Supplementary Figure 4

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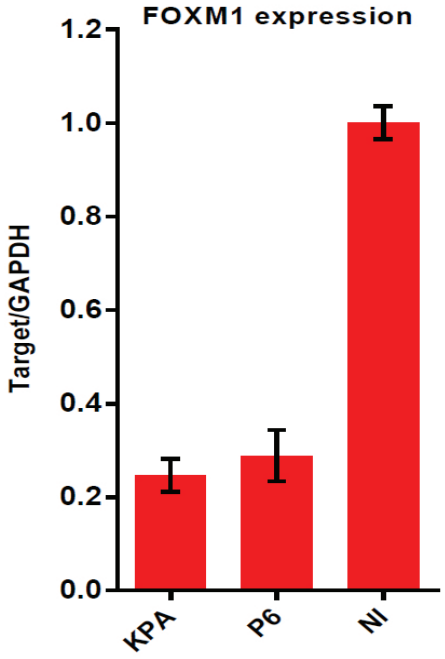

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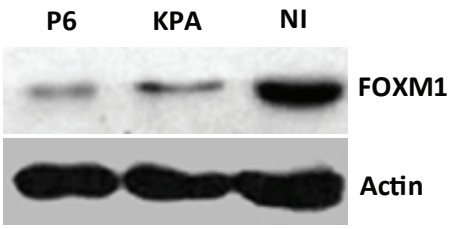

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