

**Table S1.** Selection of reference genes for treatments and time points.

Treatments	
Control	The CHGs contributing to NF3 obtained the highest rank for all algorithms and CV, but the high F values for <i>ACT</i> in comparison with those of <i>EF</i> advice to substitute <i>ACT</i> by <i>EF</i> in such three-gene combination. Thus, the NF set composed by <i>H2B</i> , <i>OUB</i> and <i>EF</i> was the best for CV and F (for one and two factors) (Table 4).
IBA	For both mono and bifactorial cases, the algorithms influenced by gene transcript co-accumulation ( <i>v.g.</i> , co-expression) usually placed <i>ACT</i> in the last position (D <sub>Co</sub> and g <sub>No</sub> ). In spite of this, in NF <sub>i</sub> cases the values for <i>ACT</i> are very close to the first ranked gene. In the other hand, the methods avoiding co-accumulation influences (CV/F and BKS) advise the use of NF3 (which includes <i>ACT</i> transcript accumulation values). Also, NF3 is better ranked than gene sets containing additional CHGs (Fig. 4). By these reasons the use of NF3 for IBA treatment is advised.
IBA+SHAM	The combination <i>H2B/ACT</i> (NF2) seems a good compromise among all methods for the monofactorial case. The inclusion of a third gene such as <i>EF</i> may jeopardize the required real stability since it is low ranked for CV, both F and most algorithms (Table 4). What is more, the CHG set contributing to NF2 is the best ranked for CV and both F (Fig. 4). Nevertheless, the addition of <i>OUB</i> , well ranked for CV and F in the bifactorial case, to contribute to NF3, will improve gene representativity without compromising NF stability (Fig 4).
Time points	
4 h	<i>GADPH</i> ranked high for all softwares, but its F value is the highest for the monofactorial case (Table 4). According to CV and F values and the preference given to CV ranking, the set composed by <i>H2B</i> , <i>OUB</i> and <i>TUA</i> seems the best combination to contribute to a NF useful for both mono and bifactorial cases (Table 4), in spite that algorithms may disagree due to the effect of co-regulation in most of them. Also, CHG set is well ranked for both cases (Fig. 4).
24 h	Although for this time point the genes contributing to NF3 are the best candidates according to CV, F and BKS, the algorithms affected by gene co-regulation display <i>EF</i> as first candidate. This possible effect of co-regulation is also supported by the results showed in Figure 1. Consequently, <i>ACT</i> , alone or in combination with <i>H2B</i> (hereby contributing to NF2) or <i>H2B</i> plus <i>OUB</i> (hereby contributing to NF3) may be considered as the best options for normalization. From those possibilities, <i>ACT</i> and NF2 obtained the best positions when considering together CV and F rankings (Fig 4). As far as these two possibilities do not differ too much in these rankings from NF3, which is more representative, we consider NF3 as the best option for normalization in 24 h time point, at least for the monofactorial case. In the bifactorial case, a conflict between NF3 genes and the combination <i>ACT</i> , <i>H2B</i> and <i>EF</i> may exist (Table 4). Since there are no co-regulation algorithm interactions for CV/F method, by suppressing <i>GADPH</i> from this comparison it is possible to appreciate that NF3 keeps better the requirements for selection.
48 h	It seems clear that genes composing NF3 constitute the best three-CHG set for normalization in both mono and bifactorial cases.
96 h	Although CV/F based considerations leads to propose again NF2 as the best alternative –in this occasion supported by all co-regulation influenced algorithms–, results comparing gene sets (Fig. 4) advice the use, in both mono and bifactorial panels, of a CHG set also comprising <i>EF</i> , furthermore more in agreement with all algorithms. In spite of <i>EF</i> is not well ranked in F for the monofactorial case, its instability value is comparatively low (Table 4).