

**Supplementary Table S1.** Fold changes in embryos at the pluteus stage, deriving from sea urchins exposed to PAHs and PCBs, (in red down-expressed genes; in green up-expressed genes) in comparison with the control (represented by embryos deriving from adults of sea urchins reared non-contaminated mesocosm) at 48 hpf. Fold differences greater than  $\pm 1.5$  were considered significant. The genes were grouped according the three functional classes: stress, development/differentiation and detoxification.

		<i>PAHs</i>	<i>PCBs</i>
<i>Stress</i>	<i>ChE</i>	-5.976	-5.870
	<i>CYP-2UI</i>	2.808	2.977
	<i>GAPDH</i>	-2.018	-2.028
	<i>GST</i>	7.307	7.372
	<i>HSP75</i>	-4.736	-3.083
	<i>Hsp90</i>	-2.337	-2.371
	<i>PKS</i>	-8.996	-6.475
	<i>SULT1</i>	-9.998	-9.287
	<i>TNF</i>	5.633	8.084
<i>Development/Differentiation</i>	<i>CM-K</i>	1.917	3.980
	<i>CREB</i>	5.407	6.902
	<i>EGF</i>	1.810	5.823
	<i>FZ-7</i>	-1.453	3.710
	<i>HH</i>	5.344	1.790
	<i>JAK</i>	4.412	3.314
	<i>Lefty</i>	-4.885	-4.797
	<i>M-Vg1</i>	2.433	2.384
	<i>NLK</i>	2.182	8.600
	<i>NOTCHLESS</i>	3.543	7.827
	<i>PLAUF3</i>	2.399	2.125
	<i>PLC</i>	8.740	8.440
	<i>Ptc</i>	-5.741	-2.837
	<i>Smo</i>	-6.852	-5.311
	<i>STAT1</i>	0.898	5.886
<i>Detoxification</i>	<i>NADH</i>	-1.889	-2.757

**Supplementary Table S2.** Gene name and acronym of genes from *Paracentrotus lividus* and their human orthologs used for Network analysis. The genes included in the stress response and development/differentiation networks are highlighted in red and blue, respectively.

Gene name	<i>Paracentrotus lividus</i>	<i>Homo sapiens</i>
<i>Cholinesterase</i>	<i>ChE</i>	<i>BCHE</i>
<i>Cytochrome P450 2UI isoform X2</i>	<i>CYP-2UI</i>	<i>CYP4F12</i>
<i>Glutathione-S-transferase</i>	<i>GST</i>	<i>GSTK1</i>
<i>Glyceraldehyde-3-phosphate dehydrogenase</i>	<i>GAPDH</i>	<i>GAPDH</i>
<i>Heat shock protein 75</i>	<i>hsp75</i>	<i>TRAP1</i>
<i>Heat shock protein 90</i>	<i>hsp90</i>	<i>HSP90AA1</i>
<i>NADH dehydrogenase</i>	<i>NADH</i>	<i>NDUFS1</i>
<i>Polyketide synthase</i>	<i>PKS</i>	<i>ARAF</i>
<i>Sulfotransferase 1C2-like</i>	<i>SULT1</i>	<i>SULT1A1</i>
<i>Tumor necrosis factor alpha</i>	<i>TNF</i>	<i>TNF</i>
<i>Calcium/calmodulin-dependent protein kinase</i>	<i>CM-K</i>	<i>CALM1</i>
<i>Camp-responsive element</i>	<i>CREB</i>	<i>CREB1</i>
<i>Epidermal growth factor</i>	<i>EGF</i>	<i>EGF</i>
<i>Frizzled7</i>	<i>FZ-7</i>	<i>FZD7</i>
<i>Hedgehog</i>	<i>HH</i>	<i>SHH</i>
<i>Janus kinase</i>	<i>JAK1</i>	<i>JAK1</i>
<i>Lefty</i>	<i>Lefty</i>	<i>RTTN</i>
<i>Maternal Vg1</i>	<i>M-Vg1</i>	<i>TAB1</i>
<i>Nemo-like kinase</i>	<i>NLK</i>	<i>NLK</i>
<i>Notchless protein</i>	<i>NOTCHLESS</i>	<i>NLE1</i>
<i>Patched</i>	<i>Ptc</i>	<i>PTCH1</i>
<i>Phospholipase C</i>	<i>PLC</i>	<i>HSPG2</i>
<i>PLAUF 3 RNA-binding protein AUF1 mRNA</i>	<i>PLAUF3</i>	<i>SLBP</i>
<i>Signal transducer and activator of transcription</i>	<i>STAT1</i>	<i>STAT1</i>
<i>Smoothened</i>	<i>Smo</i>	<i>SMO</i>

**Supplementary Table S3.** Gene name, acronym, function and reference of new twenty-five genes.

Gene name	Acronym	Function	References
<i>Calcium/calmodulin-dependent protein kinase type 1D</i>	CM-K	Calcium-binding protein that is present in eggs and involved in the control of nuclear envelope breakdown (NEB) during mitotic division	[1,2]
<i>Camp-responsive element</i>	CREB	Transcription factor that binds certain DNA sequences, named cAMP response elements (CRE), increasing or decreasing the expression of target genes	[3]
<i>Cholinesterase</i>	ChE	Protein belonging to a group of esterases expressed in response to environmental stresses	[4,5]
<i>Cytochrome P450 2UI isoform X2</i>	CYP-2UI	This gene encodes for heme-thiolate monooxygenase enzymes, which are involved in stress response	[6,7]

<i>Epidermal growth factor</i>	<i>EGF</i>	Growth factor that regulates various aspects of cell growth, differentiation and morphogenesis during embryo development	[8–10]
<i>Frizzled7</i>	<i>FZ-7</i>	Binding to Wnt6, this receptor is responsible for initiating $\beta$ -catenin nuclearisation in macromeres at the 5th cleavage, which is necessary for endoderm specification	[11]
<i>Glyceraldehyde-3-phosphate dehydrogenase</i>	<i>GAPDH</i>	A glycolytic enzyme that plays a major role in the production of energy required for sperm cell movement	[12–14]
<i>Glutathione-S-transferase</i>	<i>GST</i>	This enzyme is expressed in the intestine tissue and it is involved in the response of environmental stresses	[4]
<i>Heat shock protein 75</i>	<i>hsp75</i>	<i>hsp75</i> was first described, together with <i>hsp70</i> , in relation to the heat shock stress. This protein is currently known to be also expressed in response to cold or heavy metals exposure, during oogenesis and embryo development of the sea urchin <i>P. lividus</i>	[15,16]

<i>Heat shock protein 90</i>	<i>hsp90</i>	A family of proteins that are expressed in response to stressful conditions. <i>Hsp90</i> plays important roles in embryogenesis	[17]
<i>Hedgehog</i>	<i>HH</i>	Protein expressed downstream to Brachyury and FoxA in the endomesoderm gene regulatory network during gastrulation that participates to the mesoderm organization	[18]
<i>Janus kinase</i>	<i>JAK</i>	Transcription factor that, binding to the STAT1, plays a key role in the developmental processes	[19,20]

<i>Lefty</i>	<i>Lefty</i>	This protein, together with <i>Delta</i> and <i>Notch</i> , is involved in left-right establishment in sea urchins	[21]
<i>maternal Vg1</i>	<i>M-Vg1</i>	This gene, together with <i>Nodal</i> , is involved in ventral-dorsal establishment in sea urchins	[22]
<i>NADH dehydrogenase</i>	<i>NADH</i>	This enzyme is involved in the maintenance of cellular redox homeostasis for modulating numerous biological events. Changing its phosphorylation state, <i>NADH</i> modulates sperm motility	[23,24]
<i>Nemo-like kinase protein</i>	<i>NLK</i>	This protein, positively regulated by Delta-Notch signal, induces the specification of mesodermal cells by downregulating TCF.	[25]

<i>Notchless protein</i>	<i>NOTCHLESS</i>	Protein involved in the <i>NOTCH</i> pathway implicated in the differentiation of secondary mesenchyme cells, which are fated to produce mesodermal cells	[26,27]
<i>Phospholipase C</i>	<i>PLC</i>	An enzyme positively regulated by the <i>CM</i> signal and involved in egg activation and during embryo development in sea urchins	[28,29]
<i>PLAUF 3 RNA-binding protein AUF1 mRNA</i>	<i>PLAUF3</i>	This protein, binding to <i>H3.3 histone 3`UTR</i> , is probably implicated in mRNA instability	[30]

<i>Polyketide synthase</i>	<i>PKS</i>	The polyketide compound synthesized by PKS gene possibly has a role in the immune defense of the developing embryo	[31]
<i>Patched</i>	<i>Ptc</i>	Co-receptor of HH expressed within the neighboring skeletogenic and non-skeletogenic mesoderm	[18]
<i>Smoothed</i>	<i>Smo</i>	Developmental regulator that activates HH signaling	[32]
<i>Signal transducer and activator of transcription</i>	<i>STAT1</i>	Transcription factor that, binding to the <i>Jak</i> factor, plays a key role in the developmental processes	[19,33,34]

<i>Sulfotransferase 1C2-like</i>	<i>SULT1</i>	Enzyme that catalyzes the bioactivation of arylamines	[35]
<i>Tumor necrosis factor alpha</i>	<i>TNF</i>	Protein that restricts and terminates inflammatory responses through the modulation of the ubiquitination status of central components in <i>NF-κB</i> , <i>IRF3</i> and apoptosis signaling cascades	[36]

**Supplementary Table S4.** Gene name, acronym and reference of 62 genes.

	<b>Gene name</b>	<b>Acronym</b>	<b>Reference</b>
<b><i>Stress</i></b>	<i>ADP-ribosylation factor 1</i>	<i>ARF1</i>	[37]
	<i>caspase-8</i>	<i>CASP8</i>	[38]
	<i>Sp-Cspe3/7L</i>	<i>caspase 3/7</i>	[39]
	<i>Cytochrome b</i>	<i>cytb</i>	[40]
	<i>DNA-methyltransferase 1</i>	<i>MTase</i>	[40]
	<i>ERCC excision repair 3</i>	<i>ERCC3</i>	[41]
	<i>Glutamine synthetase</i>	<i>GS</i>	[40]
	<i>Glyoxylate reductase/hydroxypyruvate reductase</i>	<i>GRHPR</i>	[37]
	<i>Heat Shock Protein 56</i>	<i>hsp56</i>	[40]
	<i>Heat Shock Protein 60</i>	<i>hsp60</i>	[40]
	<i>Heat Shock Protein 70</i>	<i>hsp70</i>	[40]
	<i>Hypoxia inducible factor 1-alpha</i>	<i>HIF1A</i>	[39]
	<i>Nuclear factor kappa-light-chain-enhancer of activated B cells</i>	<i>NF-kB</i>	[42]
	<i>Poly(ADP-ribose) polymerase 1</i>	<i>PARP-1</i>	[37]
	<i>p38 mitogen-activated protein kinase</i>	<i>p38 MAPK</i>	[40]

	<i>Succinate dehydrogenase</i>	<i>SDH</i>	[37]
	<i>Tumor protein p53</i>	<i>p53</i>	[39]
	<i>14-3-3 epsilon protein</i>	<i>14-3-3 ε</i>	[40]
<hr/> <b><i>Development/ Differentiation</i></b> <hr/>	<i>ALG-2 interacting protein X/1</i>	<i>Alix</i>	[43]
	<i>Antidorsalizing morphogenetic protein 2</i>	<i>ADMP2</i>	[37]
	<i>Blastula protease 10</i>	<i>BP10</i>	[40]
	<i>Blimp</i>	<i>Blimp</i>	[43]
	<i>Brachyury</i>	<i>Bra</i>	[37]
	<i>Cadherin-associated protein (catenin) delta 2</i>	<i>δ-2-catenin</i>	[39]
	<i>c-Jun N-terminal kinase</i>	<i>JNK</i>	[44]
	<i>Delta</i>	<i>Delta</i>	[37]
	<i>Forkhead box protein A</i>	<i>FOXA</i>	[44]
	<i>Forkhead box protein G</i>	<i>FoxG</i>	[44]
	<i>Forkhead box protein O</i>	<i>Foxo</i>	[44]
	<i>Goosecoid</i>	<i>Goosecoid</i>	[37]

<i>Growth factor independent 1</i>	<i>GFI1</i>	[44]
<i>Hatching enzyme</i>	<i>hat</i>	[40]
<i>Histone H3.3</i>	<i>H3.3</i>	[37]
<i>Kinesin-19</i>	<i>KIF19</i>	[37]
<i>Nodal</i>	<i>nodal</i>	[44]
<i>Notch</i>	<i>Notch</i>	[37]
<i>One Cut Homeobox 1</i>	<i>OneCut</i>	[44]
<i>Smad6</i>	<i>Smad6</i>	[37]
<i>SRY (sex determining region Y)-box9</i>	<i>sox9</i>	[40]
<i>TGF beta-activated kinase</i>	<i>TAK1</i>	[44]
<i>Transcription factor 4</i>	<i>tcf4</i>	[44]
<i>Transcription factor 7</i>	<i>TCF7</i>	[44]
<i>Vascular endothelial growth factor</i>	<i>VEGF</i>	[44]
<i>Wnt5</i>	<i>Wnt5</i>	[43]
<i>Wnt6</i>	<i>Wnt6</i>	[43]
<i>Wnt8</i>	<i>Wnt8</i>	[43]

<hr/> <b><i>Skeletogenesis</i></b> <hr/>			
	<i>Bone morphogenetic protein 5-7</i>	<i>BMP5-7</i>	[40]
	<i>Jun</i>	<i>C-jun</i>	[42]
	<i>Nectin</i>	<i>Nec</i>	[40]
	<i>Pl-p16</i>	<i>p16</i>	[45]
	<i>Pl-p19</i>	<i>p19</i>	[45]
	<i>Spicule matrix protein 30</i>	<i>SM30</i>	[40]
	<i>Spicule matrix protein 50</i>	<i>SM50</i>	[40]
	<i>Univin</i>	<i>uni</i>	[40]
<hr/> <b><i>Detoxification</i></b> <hr/>			
	<i>Catalase</i>	<i>CAT</i>	[43]
	<i>Multi drug resistance protein 1</i>	<i>MDR1</i>	[43]
	<i>Metallothionein</i>	<i>MT</i>	[40]
	<i>Metallothionein 4</i>	<i>MT4</i>	[46]
	<i>Metallothionein 5</i>	<i>MT5</i>	[46]
	<i>Metallothionein 6</i>	<i>MT6</i>	[46]
	<i>Metallothionein 7</i>	<i>MT7</i>	[46]

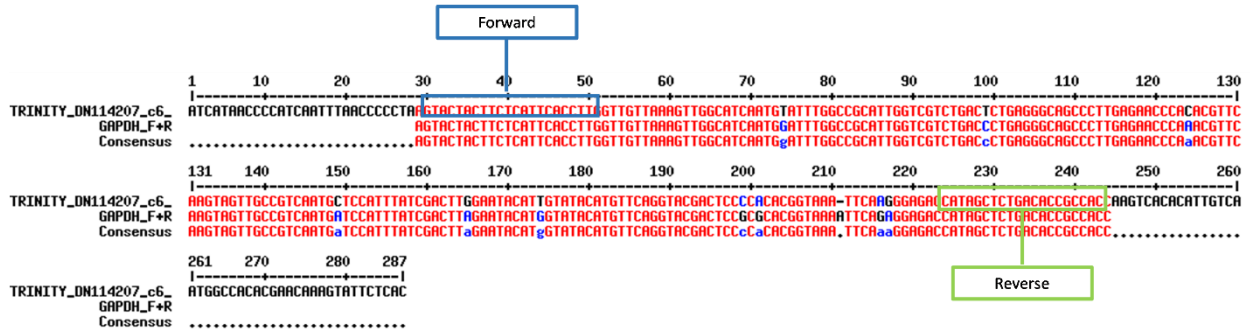
*Metallothionein 8*

*MT8*

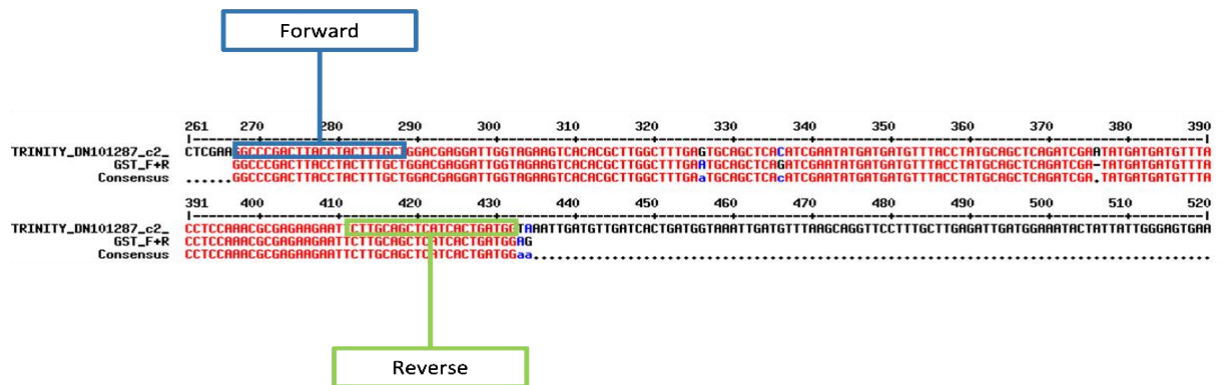
[46]

**Figure S1.** Alignments of PCR products to the original sequence of *GAPDH* (A), *GST* (B), *hsp75* (C), *TNF* (D), *CM-K* (E), *CREB* (F), *EGF* (G), *FZ-7* (H), *HH* (I), *NLK* (J), *NOTCHLESS* (K), *PLC* (L), *STAT1* (M), *NADH* (N), *ChE* (O), *Ptc* (P), *Smo* (Q), *hsp90* (R), *Lefty* (S), *PKS* (T), *CYP-2UI* (U), *SULT1* (V), *M-Vg1* (W), *JAK* (X), *PLAUF3* (Y) genes. Primers forward and reverse were reported in blu and green, respectively.

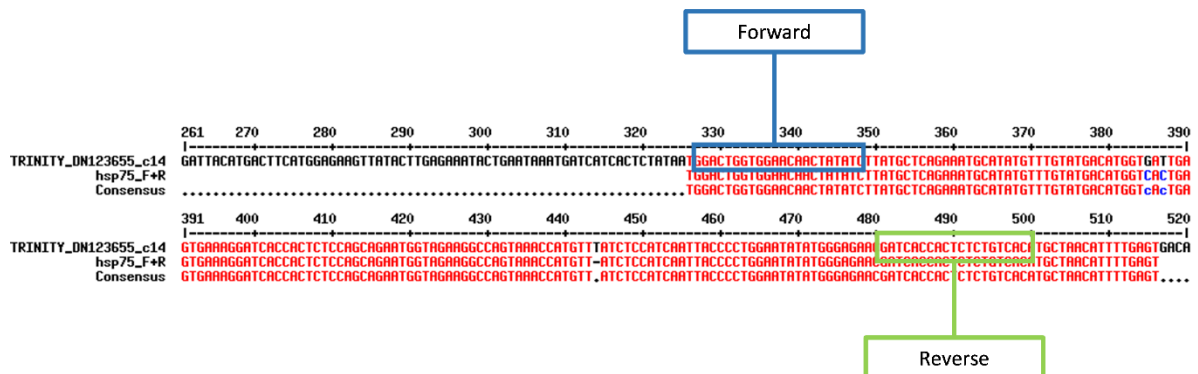
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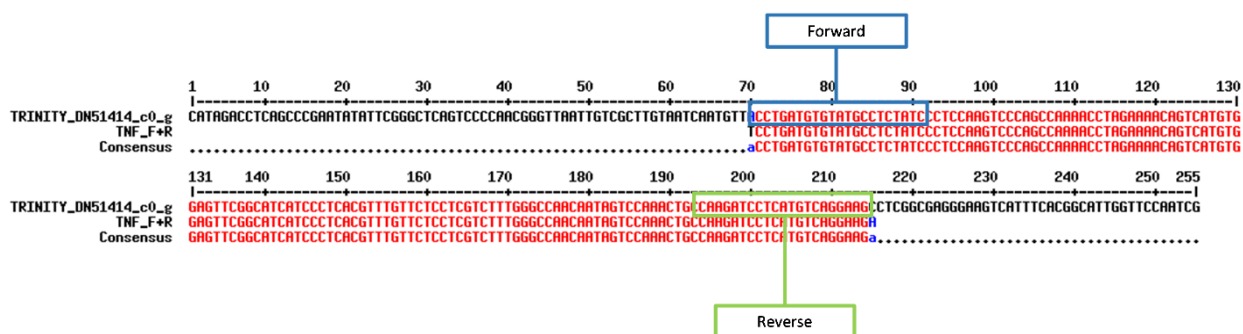
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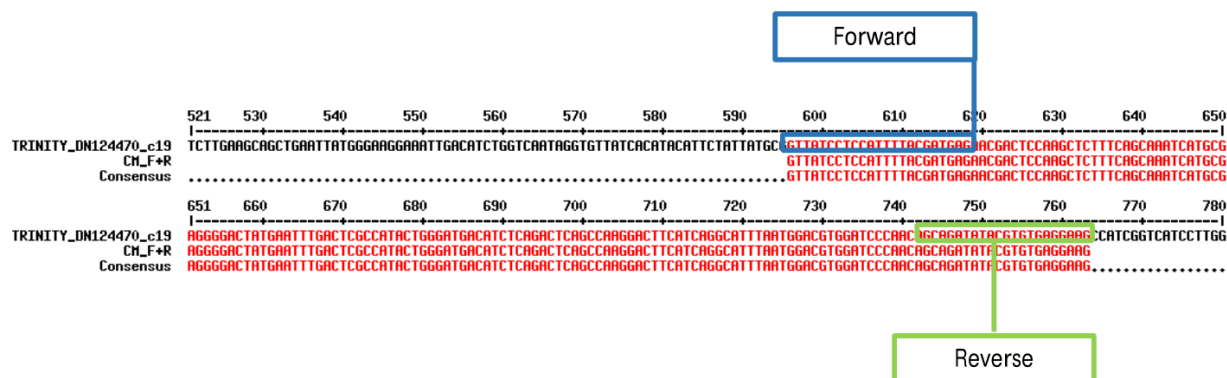
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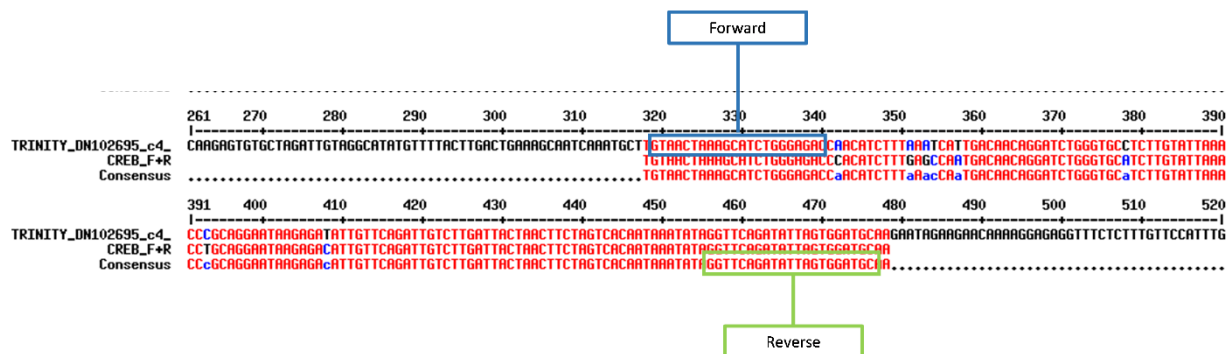
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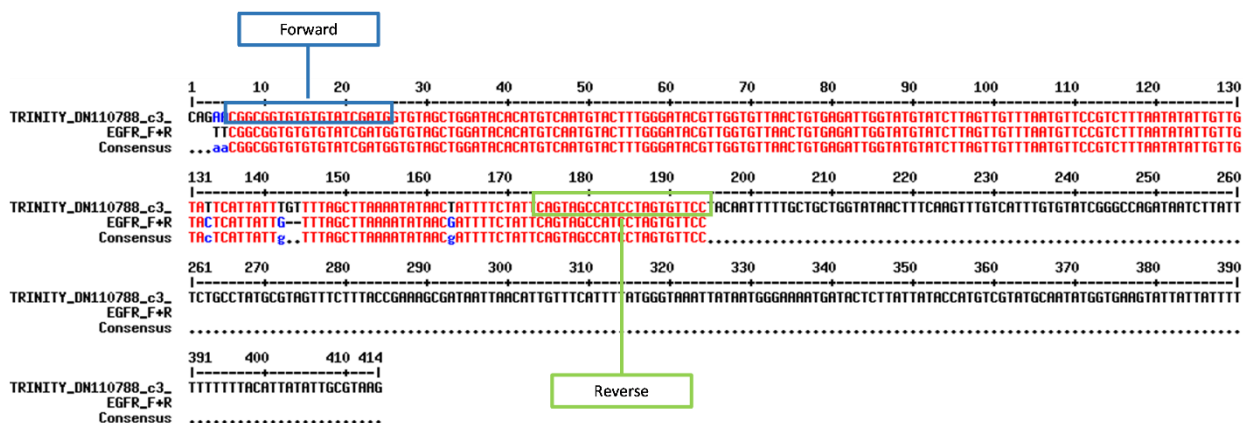
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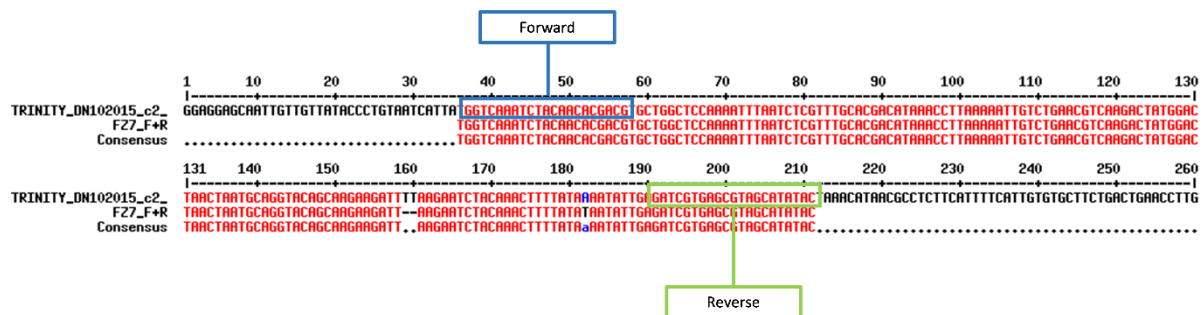
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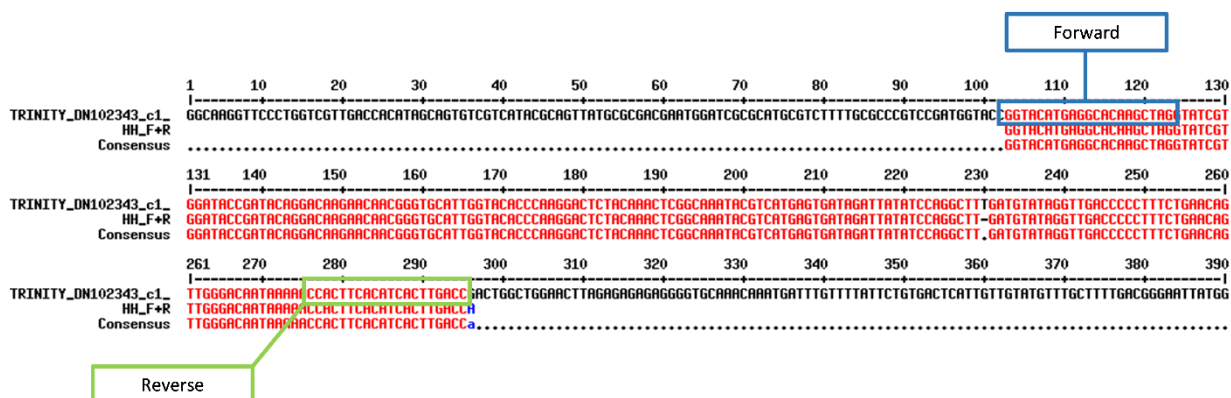
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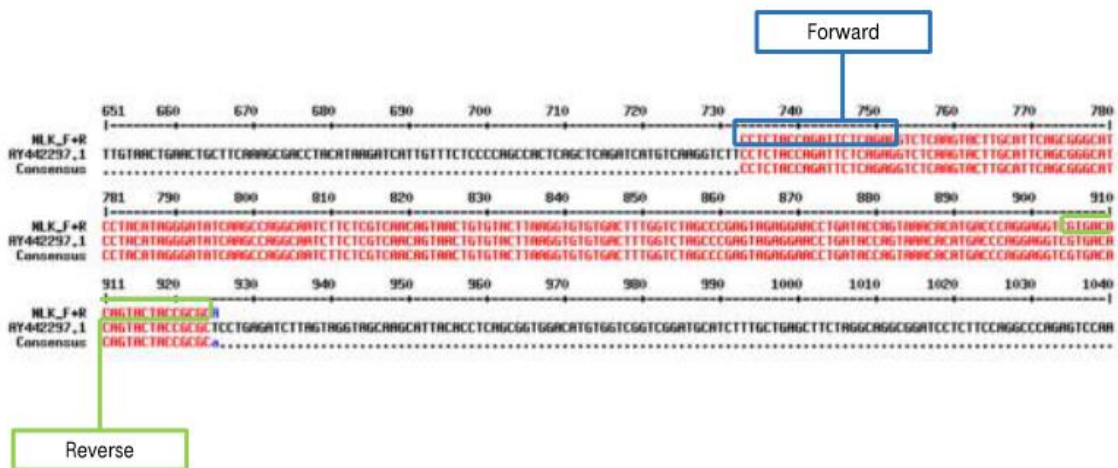
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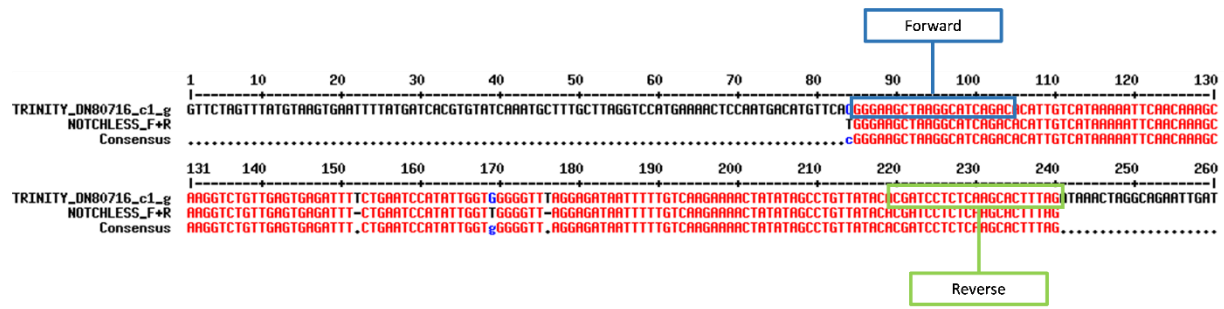
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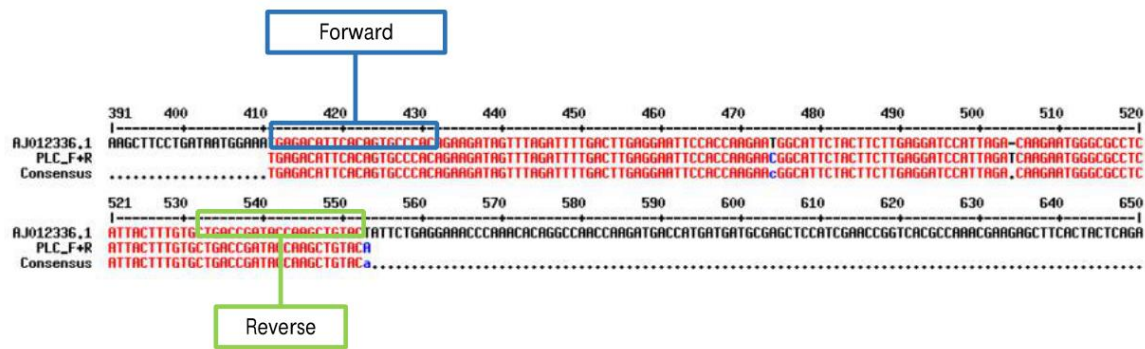
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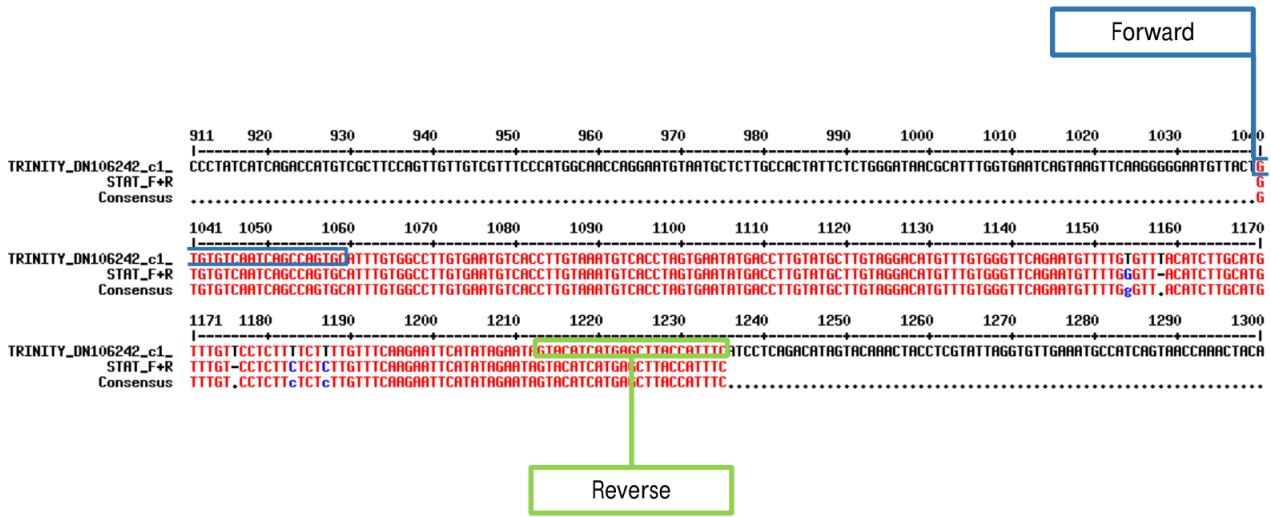
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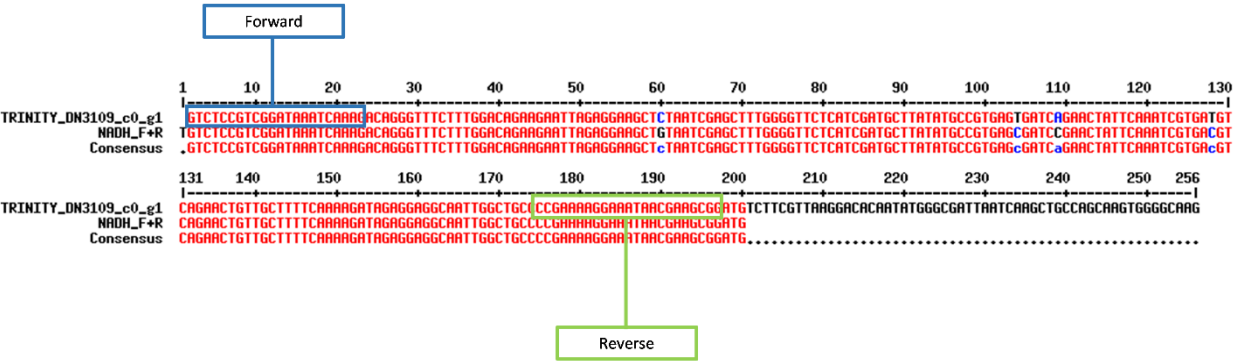
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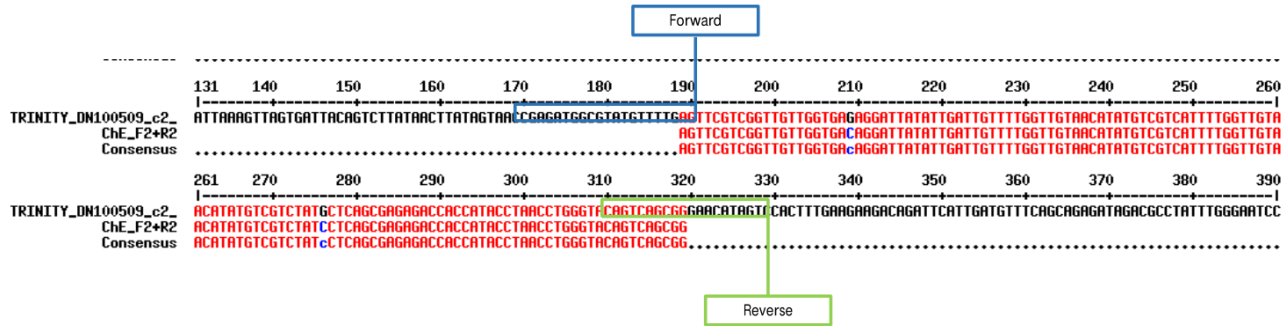
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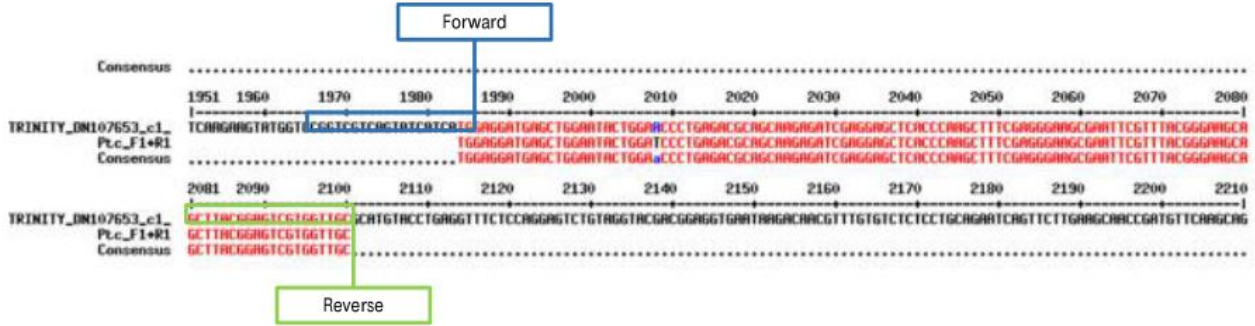
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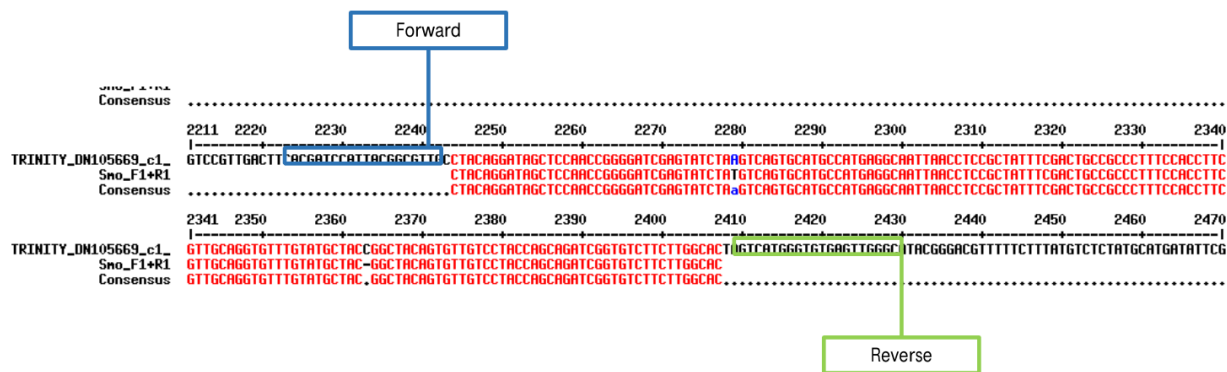
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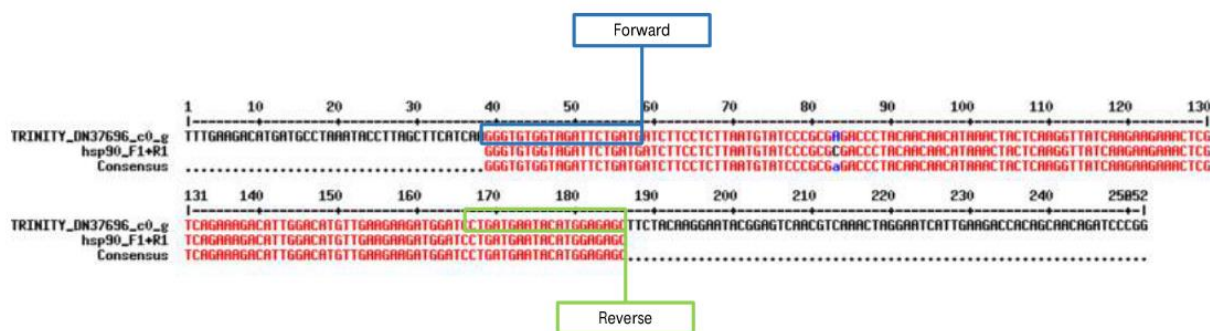
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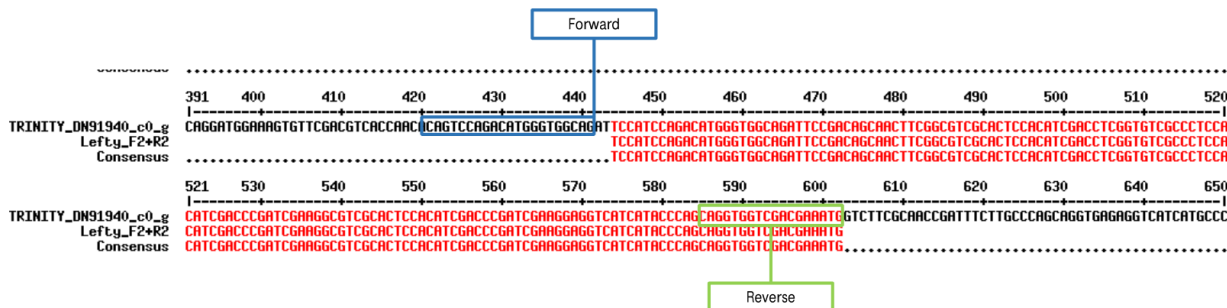
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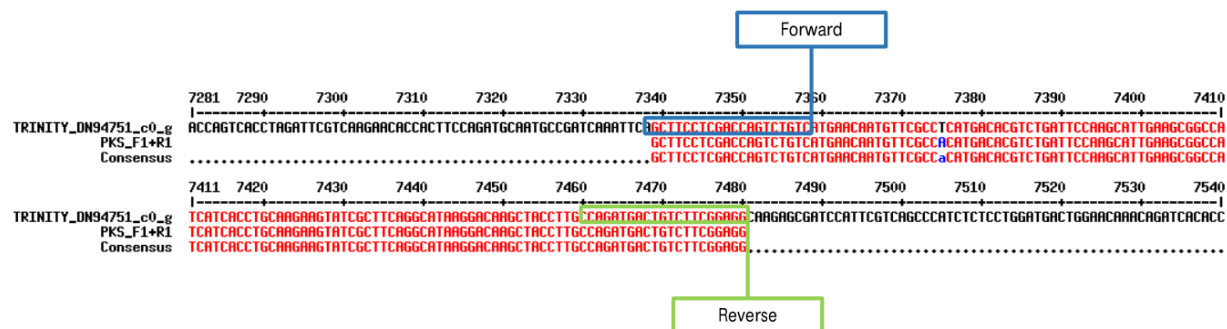
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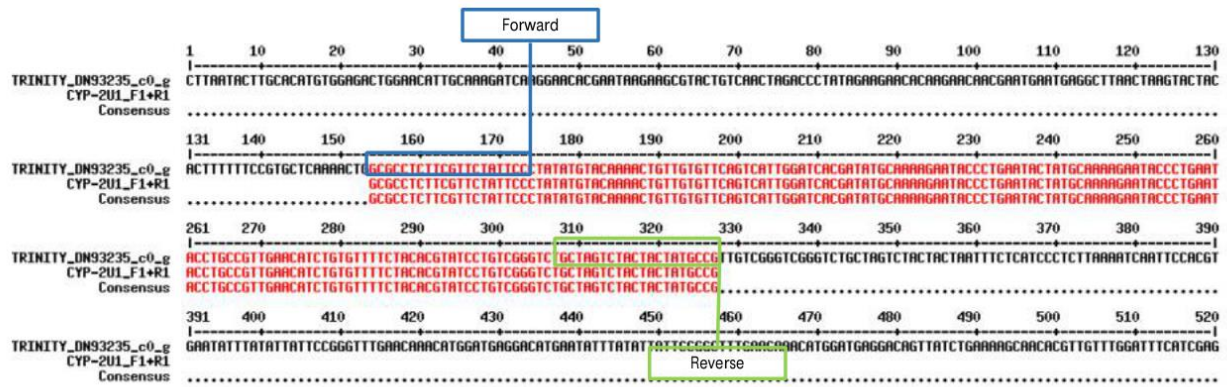
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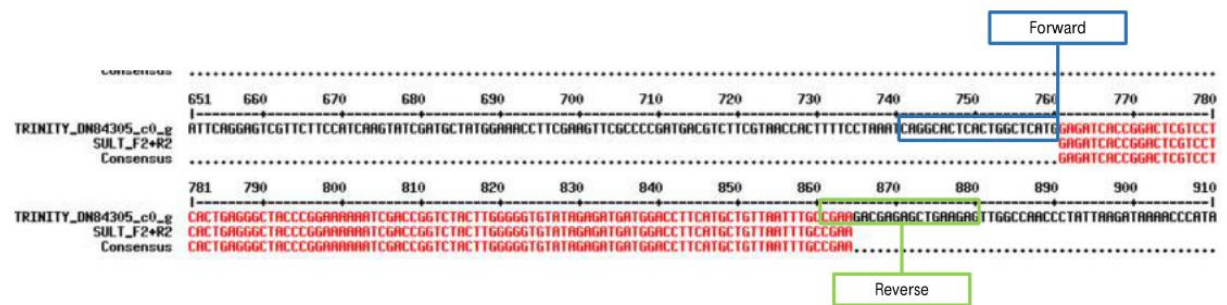
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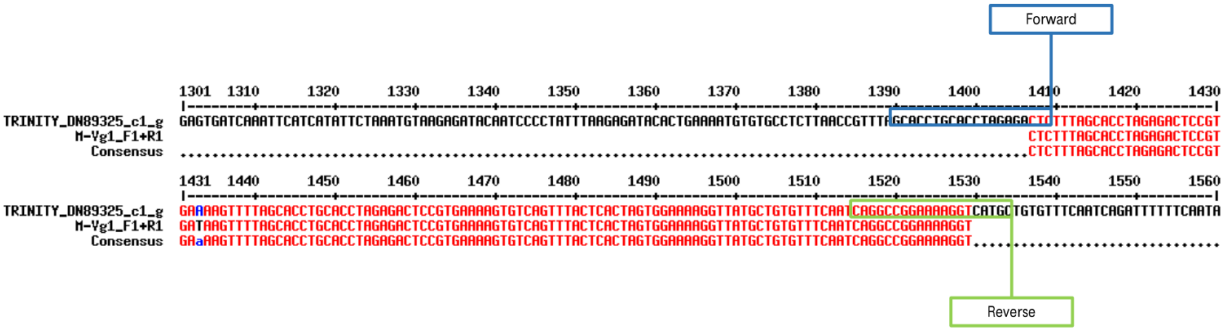
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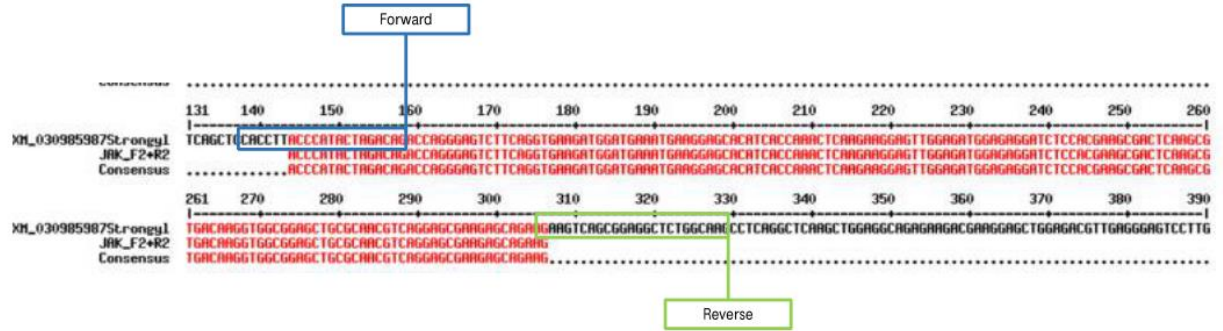
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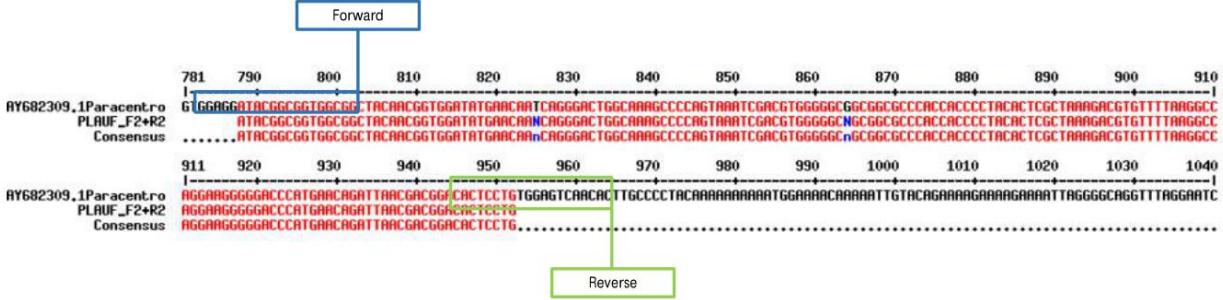
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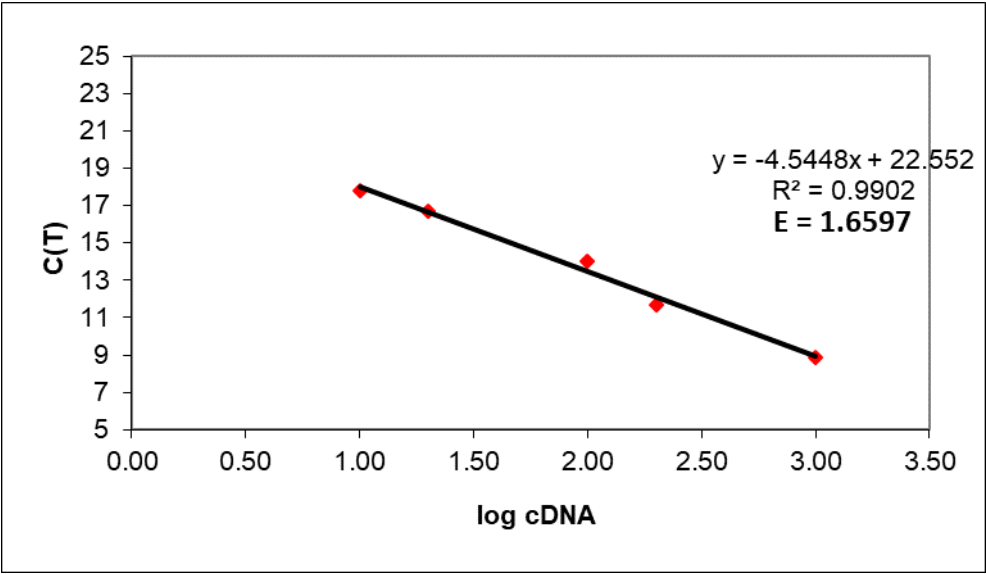


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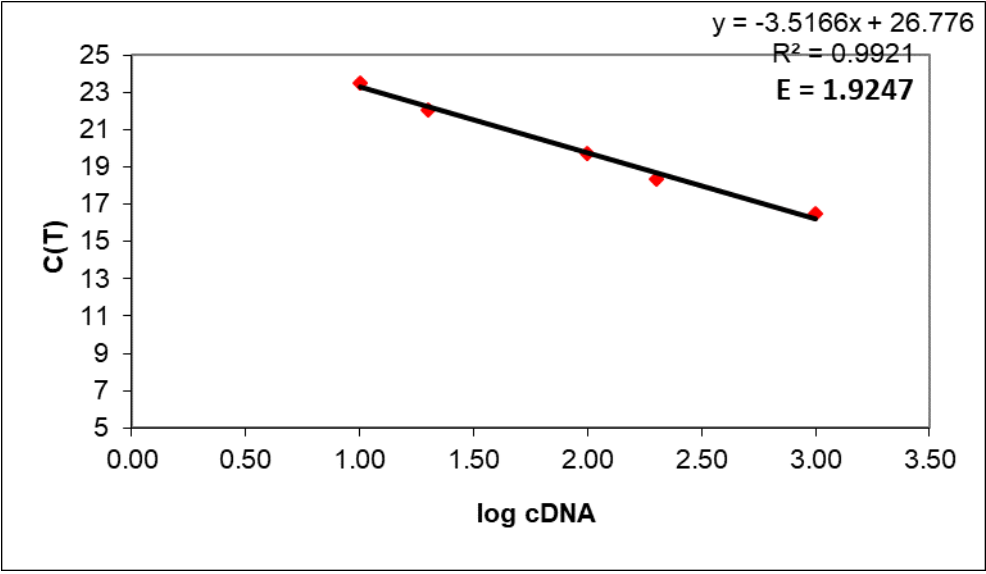


**Figure S2.** Efficiencies (E) of *18S rRNA* (A), *Ubiquitin* (B), *ChE* (C), *CREB* (D), *CYP-2UI* (E), *GAPDH* (F), *hsp90* (G), *Lefty* (H), *NLK* (I), *NOTCHLESS* (J), *PKS* (K), *PLAUF3* (L), *Ptc* (M), *Smo* (N), *SULT1* (O) genes. For those genes whose expression was detected significantly low, the efficiency was not measured.

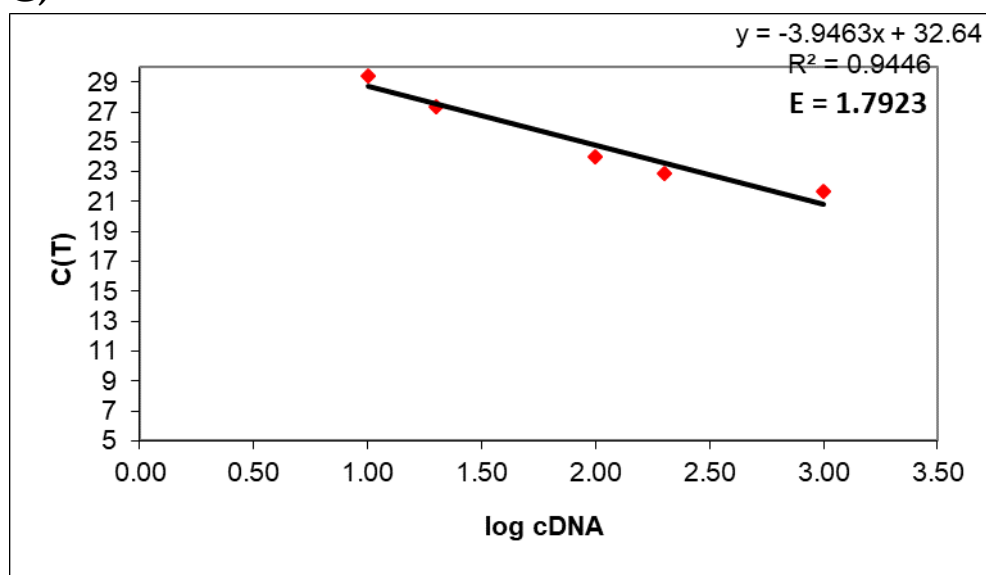
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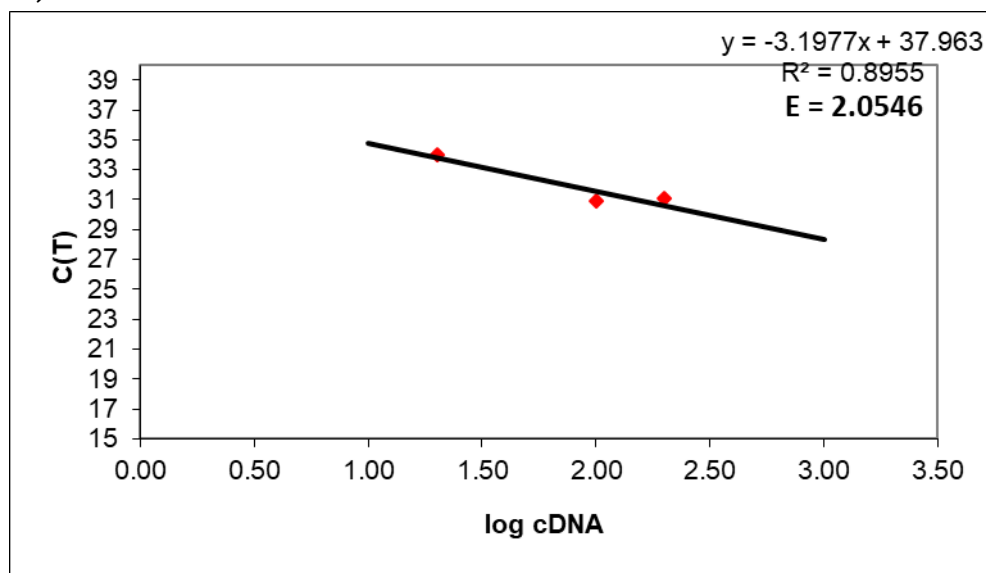
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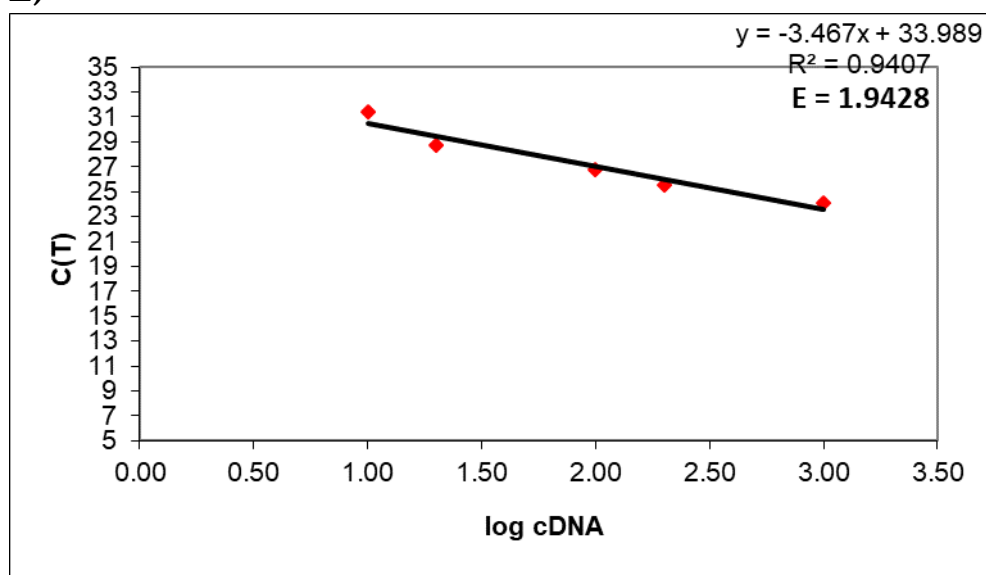
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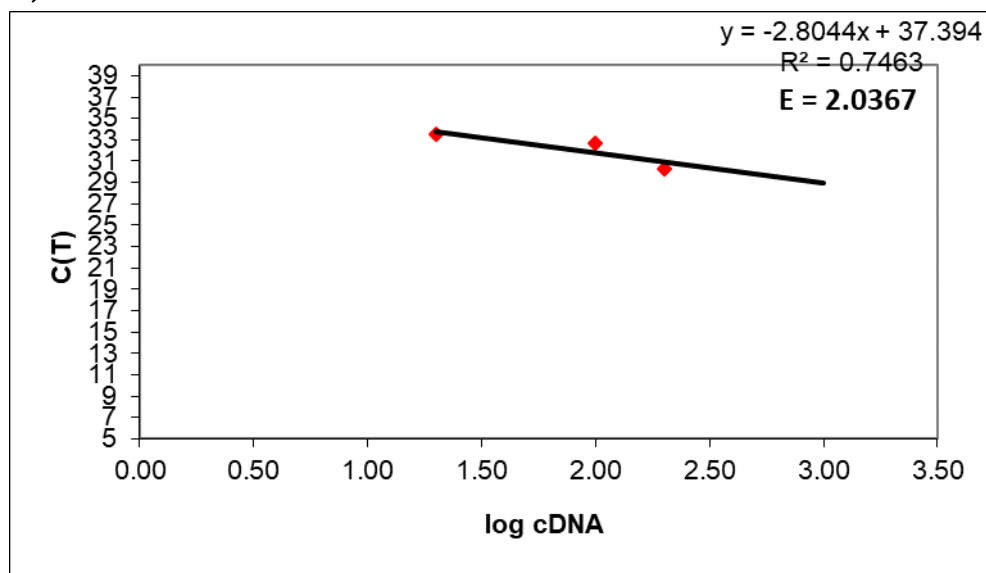
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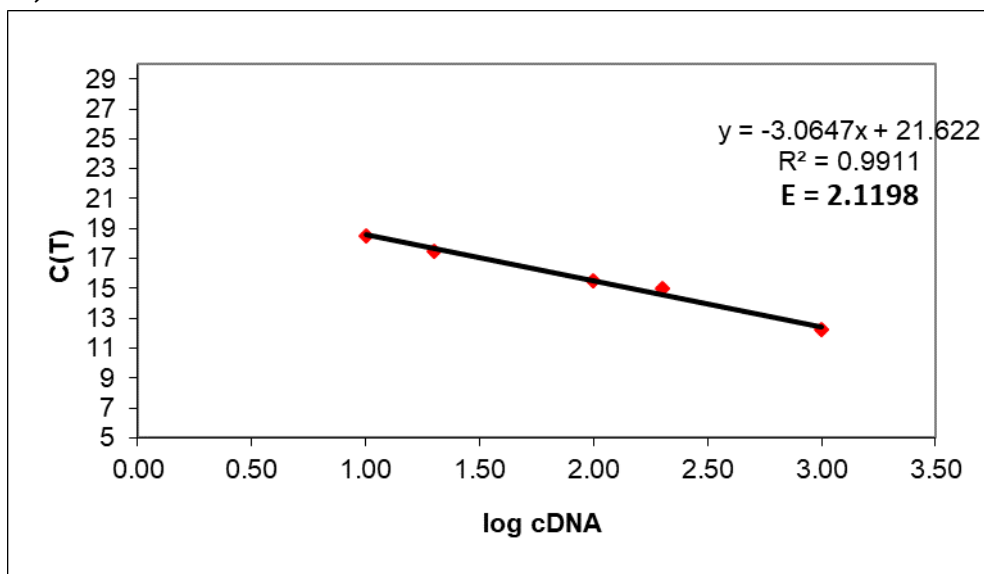
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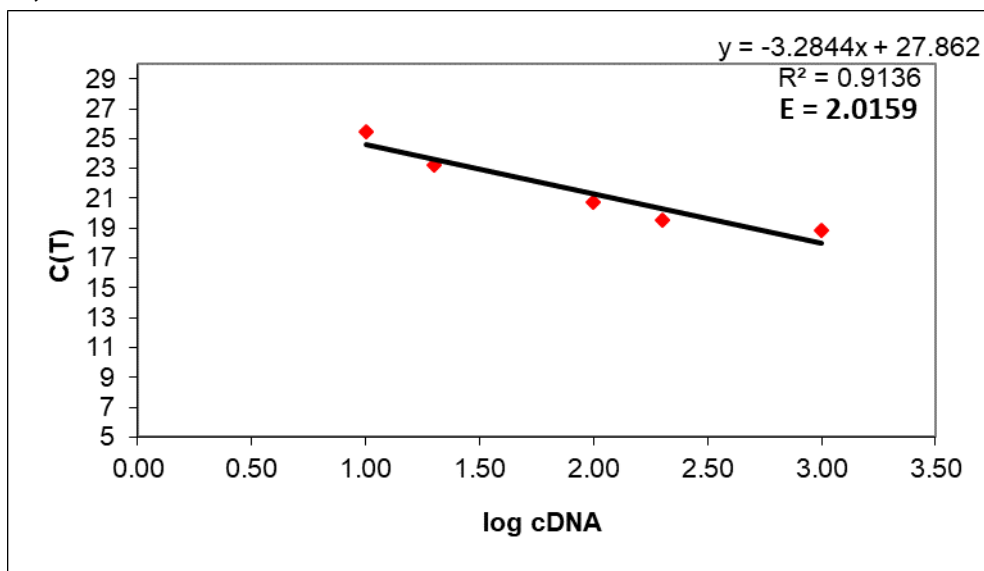
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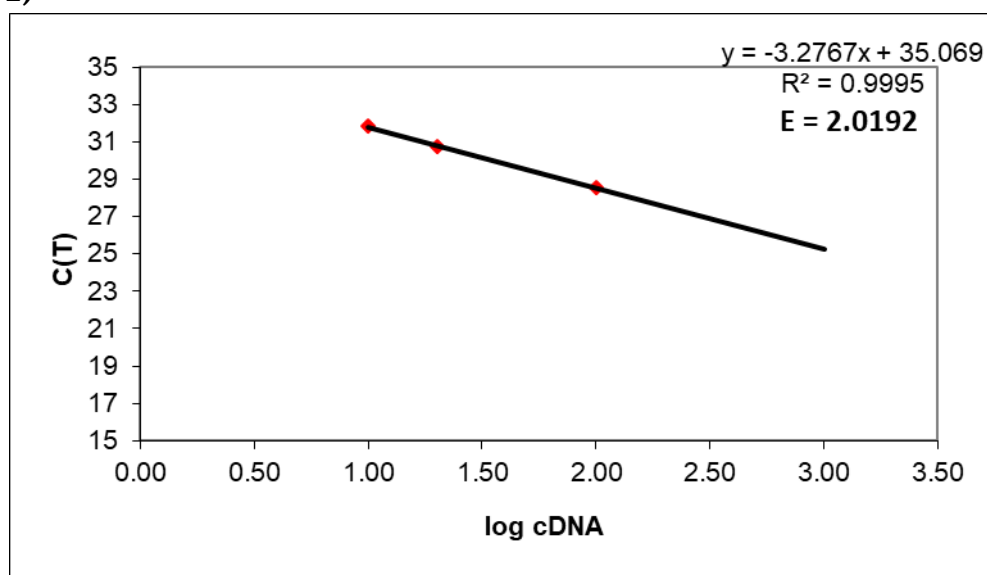
G)



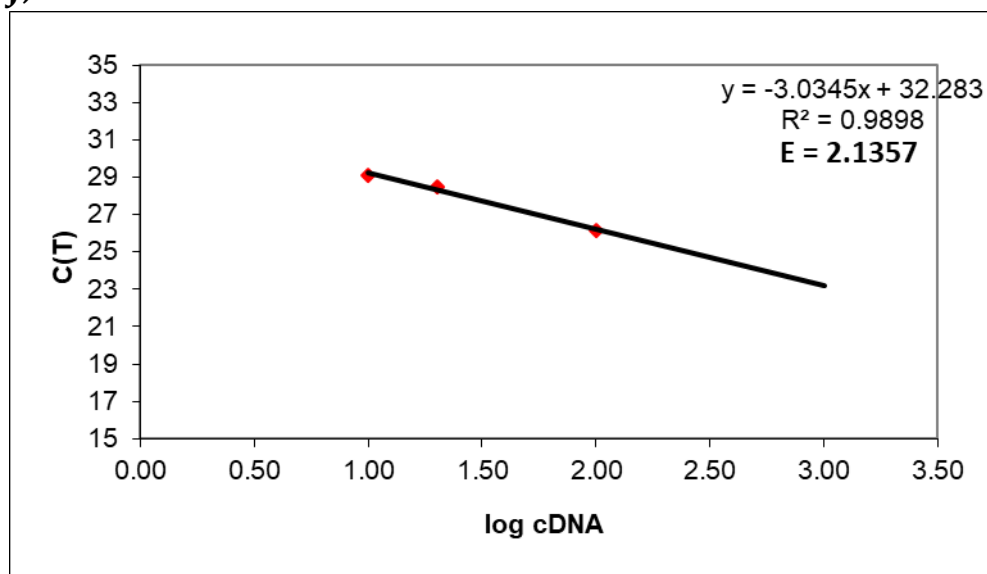
H)



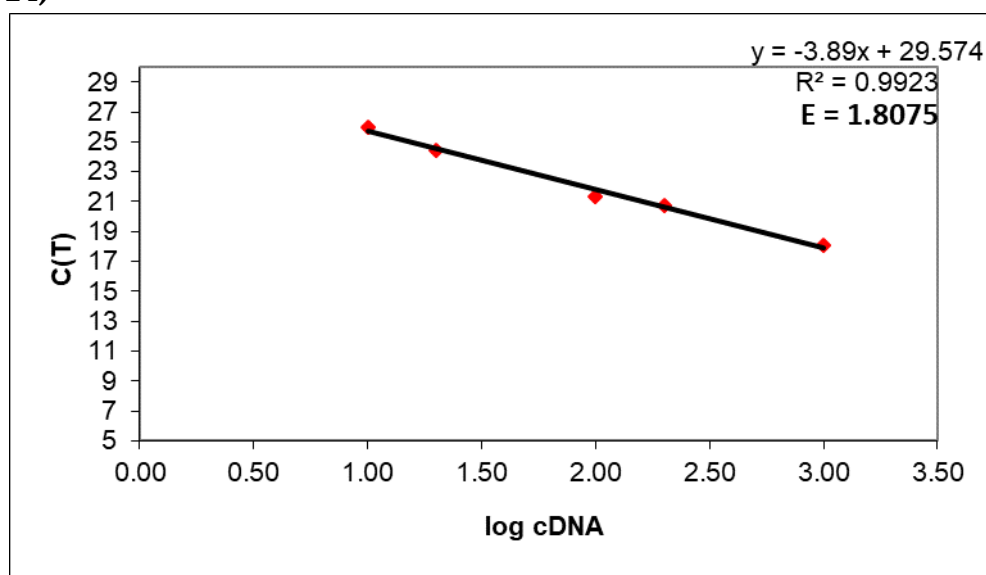
I)



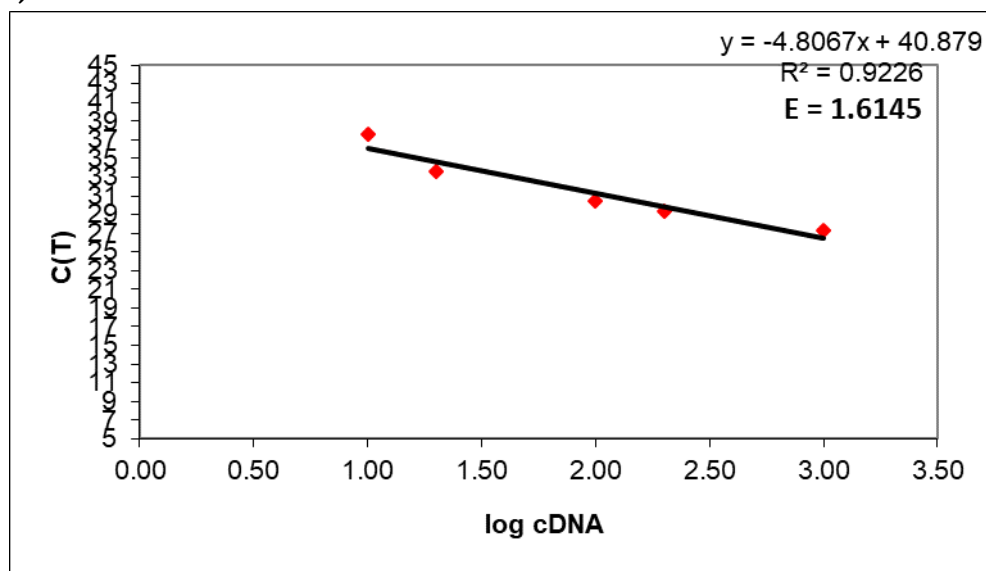
J)



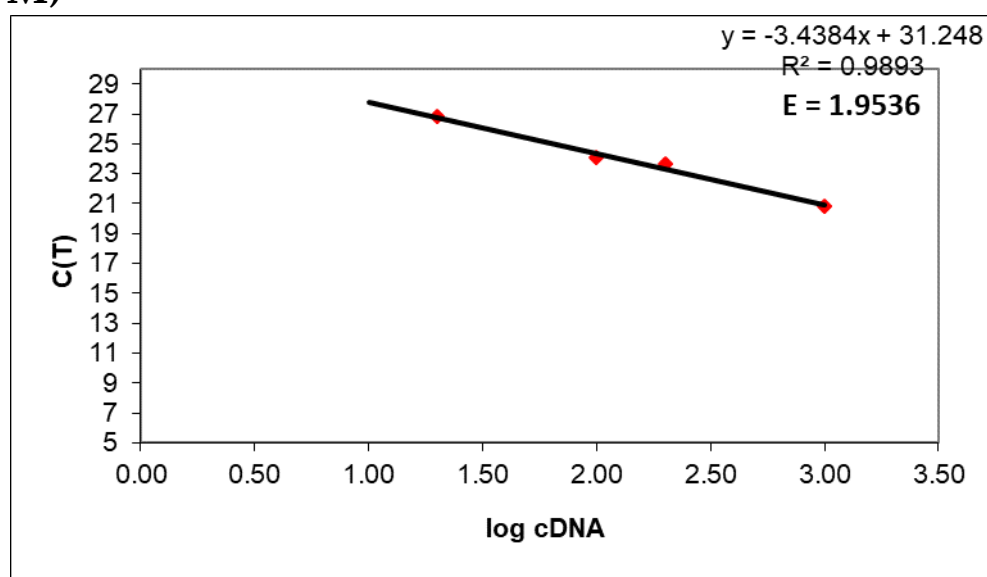
K)



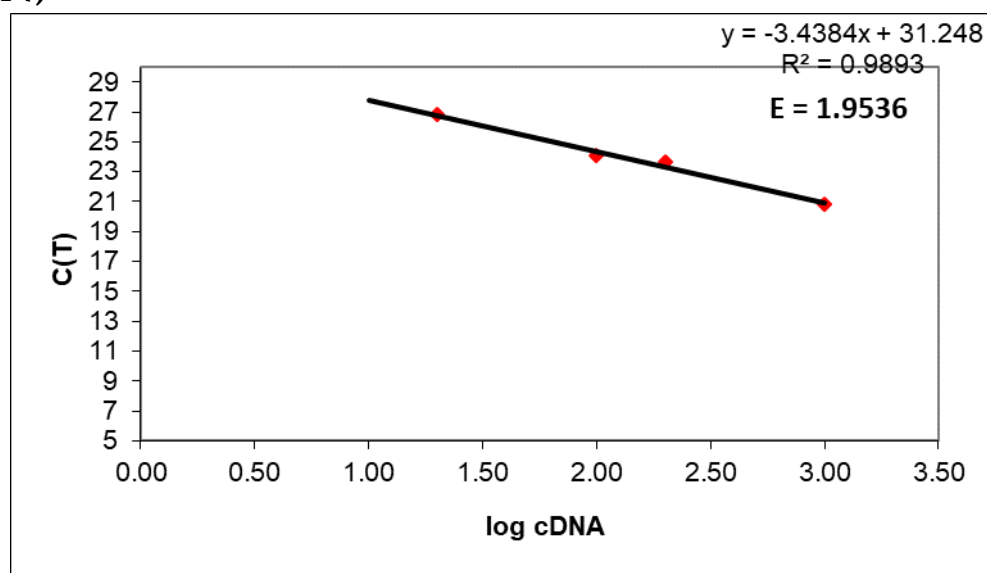
L)



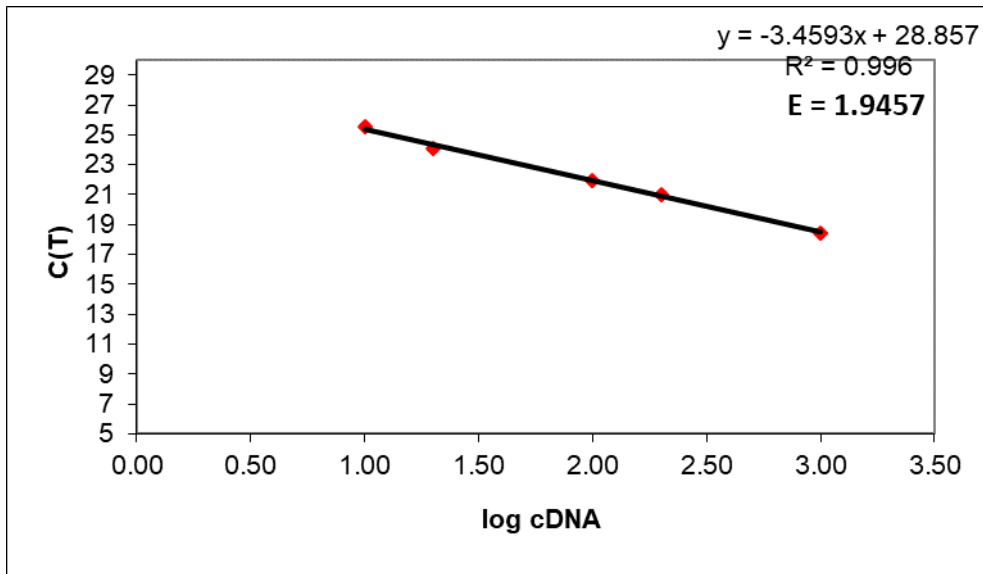
M)



N)



O)



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