評估 SARS-CoV-2 複本感染所造成之 piRNA 表現暨基因體穩衡的改變

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摘要:

細胞中 piRNA 表達的改變，除了能夠改變基因的表達外、亦被指出其能維護基因體的穩定性，進而衍生出更進一步之細胞型態改變及疾病進程。各類外界能改變 piRNA 表達的因子中，病毒因其來源及序列相似之特性，亦被指出其能影響 piRNA 之表達。而前期於各地爆發之病毒 SARS-CoV-2，其 RNA 侵入宿主細胞，造成細胞表達改變。而其與人類細胞結合位點的 S gene 之突變，則導致病毒對人類細胞的感染能力增強，也降低抗體的中和力。適以，我們將借由 SARS-CoV-2 複本的表達來瞭解其對細胞 piRNA 的調節、對基因體穩衡的影響，以及計算其可能產生的變體。我們的合作者在人類肝癌細胞 T7-Huh7 中表達 SARS-CoV-2 複本以模擬受 SARS-CoV-2 感染的細胞，並證實了 piRNA 交互作用蛋白；PIWIL4，於複本表達前後的存在。進一步，我們計算出與複本可能有直接作用的 piRNAs，並篩選複本表達前後具明顯改變的 piRNAs。而由普查已發表之基因序列，我們發現了 SARS-CoV-2 複本的表達實際上是限制了基因變異的產生，而其對基因體穩衡之影響則待更進一步闡明。先前的研究證明，在小鼠細胞內剔除 PIWIL2 會降低對 SARS-CoV-2 的免疫作用調節，我們則證明相對於 PIWIL2，PIWIL4 在人體內扮演著相似的角色，現則正於適用的人類細胞中對其進行剔除，而後確認 SARS-CoV-2 的感染是否對老化相關之 piRNAs 產生相互作用。

Assessment of SARS-CoV-2 infection affected piRNA expression and genome instability

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Abstract:

Changes of piRNA expression in cell not only affect global gene expression, maintain the genomic stability but might as well prevent the diseases' progression. Due to the sequence homology and evolutionary history, the viral infection was proposed to be one the environmental factors that interfere the piRNA expression. SARS-CoV-2 had broken out around the world through transmitted sense RNA and is capable to change cellular gene expression. The mutation of the S gene located at the site of binding to human cells which leads the virus to infect human cells. Therefore, we are going to assess the piRNA-regulated genome stability under the interference of expressed SARS-CoV-2 replicons. We found that, the expression of SARS-CoV-2 replicons does not change the expression of piRNA interacting protein, *PIWIL4*. Specific piRNAs expressional changes were detected before *versus* after the expression of replicons. From the downloaded RNA-sequencing data, we found that the transcriptional variations were limited after the viral infection. Since *PIWIL2*-knockout in mice cells limited immuno-induction capability of the secreted exosome, we are currently knocking-out the human homolog *PIWIL4* and *L1TD1* genes in order to recapitulate these observation in human cells, and confirm whether SARS-CoV-2 infection interfered with somatic piRNAs.