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Exploiting the role of exosomes and microRNAs (miRNAs) for pancreatic cancer therapy

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We have conducted a study where the expression analysis of miR-21/miR-221 in conditioned media (exosomes collected from the conditioned medium) derived from PSCs/CAF cells and PSCs/CAF cells were used for further mechanistic experiments where the miRNA was assessed by quantitative RT-PCR in addition to multiple molecular approaches. In the current presentation, I will discuss the results of our study where the expression analysis of miR-21/miR-221 showed up-regulation in the exosomes. In addition, miR-21 expression in stellate cells derived from normal pancreas was substantially lower when compared to PSCs or CAF cells derived from tumors. COLO-357 PC cells cultured in the presence of conditioned media derived from PSC/CAF cells led to a significant increase in clonogenicity and pancreatosphere formation. Furthermore, inhibition of miR-21 with antisense oligonucleotide (ASO) transfection resulted in decreased migration/invasive capacity of PSCs. Similarly, the effect of ASO-miR-221 transfection in CAF cells reduced the expression of NF-kB and K-Ras (target of miR-221) along with inhibition of migration/invasion. Moreover, miRNA expression profiling of PSCs, MIAPaCa-2 and COLO-357 cells and further validation by real time PCR, showed several differentially expressed miRNAs among which four was significantly up-regulated. In summary, these results suggest a crosstalk between PSCs/CAF cells and PC cells mediated through exosomes, resulting in the up-regulation of miR-21/miR-221 expression which in part may confer aggressiveness to PC. From these results, I will conclude that targeting these miRNAs could be useful for developing precision medicine for the prevention of tumor progression and/or for the treatment of PC.

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Gonadal tumors arising in XY pure gonadal dysgenesis

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46 XY pure gonadal dysgenesis known as Swyer syndrome is a disorder of sexual differentiation characterized by the association of a female phenotype and a 46 XY karyotype with fibrous gonads. It is generally revealed by a primary amenorrhea. This syndrome represents a ground of predilection for the development of germ cell tumors. We present the clinical, sonographic and endocrine findings in 10 cases of Swyer syndrome managed in Charles Nicolle University Hospital Tunis, Tunisia. We study the risks of malignant transformation and analyze the histopathological findings of the tumors arising on these dysgenesis gonads. The treatment options and the follow up are discussed through this largest series in the world. A bilateral gonadectomy was decided by laparoscopy in nine cases and by laparotomy for adnexal torsion of a 20 cm tumor in one case. Histopathology showed: fibrous gonads in five cases, a bilateral gonadoblastoma in three cases and a dysgerminoma associated to a gonadoblastoma in two cases. The presence of Y chromosome in the karyotype of a patient presenting a gonadal dysgenesis must lead to prophylactic bilateral gonadectomy in order to avoid a malignant transformation. Gonadectomy must be followed by a hormone replacement therapy. A screening of similar cases in sisters is imperative.

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