



Title	MicroRNA-21 promotes survival but not functional maturation of human embryonic stem cell-derived cardiomyocytes (hESC-CMs)
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Gastrointestinal follicular lymphoma: a retrospective analysis of 16 cases

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Objective: To investigate the clinical behaviour, treatment response, and prognosis of primary gastrointestinal follicular lymphoma.

Method: Clinical records of all follicular lymphoma diagnosed at Queen Mary Hospital from 1988 to 2008 were reviewed. Cases with gastrointestinal tract as the only or predominant site of involvement at presentation were considered to be primary gastrointestinal follicular lymphoma. Patient demographics, disease staging, treatment and outcome were analysed.

Results: There were 155 cases of follicular lymphoma diagnosed from 1988 to 2008, of which 123 cases were nodal and 32 cases were extranodal. Sixteen cases of primary gastrointestinal follicular lymphoma were identified, constituting 10.3% (16/155) of all follicular lymphomas, and 50% (16/32) of extranodal follicular lymphomas. There was a slight male predominance (male:female=1.67:1), presenting at a median age of 60.5 (28-85) years. The majority of patients (12/16, 75%) presented with advanced Ann-Arbor stage (stage III or IV). The Follicular Lymphoma International Prognostic Index was evaluated in 13 cases, and seven (53.8%) patients were classified as high-risk. Common primary sites were ileum (n=6), colon (n=5), and duodenum (n=3). The complete remission rate after first-line chemotherapy was 43.7% and the median duration of progression-free survival was 19 (1-156) months. The median overall survival was 54.5 (8-264) months. At a median follow-up of 93 (16-267) months, five patients had died—four from unrelated diseases and one from refractory lymphoma. The median progression-free survival of nodal follicular lymphoma in this cohort was 23.5 (1-228) months and median overall survival was 76 (5-790) months.

Conclusions: The gastrointestinal tract was the most common site of extranodal follicular lymphoma. In this cohort, primary gastrointestinal follicular lymphoma had a worse clinical outcome as compared with nodal follicular lymphoma.

microRNA-21 promotes survival but not functional maturation of human embryonic stem cell-derived cardiomyocytes (hESC-CMs)

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Purpose: microRNAs (miRNAs) are naturally occurring small non-encoding RNAs (22 nt) which negatively modulate gene expression via mRNA degradation and translational repression. Studies suggested that miRNAs are important in both normal cardiogenesis and pathogenesis of the failing heart. miRNA-21 is among those that are differentially expressed, according to our miRNAs profiling, and we hypothesised that its expression level may play a part in functional maturation of human embryonic stem cell-derived cardiomyocytes (hESC-CMs).

Methods: miRNA profiling was performed to identify differential expression of miRNAs in human embryonic stem cells (hESCs), hESC-derived, fetal (hF) and adult (hA) ventricular cardiomyocytes (VCMs). Overexpression and knockdown of miRNA-21 were achieved by lentivector (LV)-based system. To functionally characterise maturity, whole-cell patch-clamp probing for the action potential (AP) profile, and cytosolic Ca²⁺ transients measurement were performed in control versus miRNA-21 overexpressed/knockdown hESC-CMs. Contractile protein and sarcoplasmic reticulum (SR) Ca²⁺ handling protein expression were quantified with qPCR.

Results: miRNA-21 was highly expressed in hESC and hESC-VCMs; repressed in hF-VCMs and hA-VCMs. We hypothesised its expression level might be associated with functional maturity. However, we did not find any significant functional changes of hESC-CMs by manipulating its expression. The expression of contractile protein and SR Ca²⁺ handling protein was not affected, consistent with the functional data. Previous studies suggested pro-survival effects of miRNA-21 overexpression during compensatory cardiac hypertrophy. We performed TUNEL assay and found that overexpressing miRNA-21 in hESC-CMs significantly protected the cells against apoptosis induced by hydrogen peroxide challenge.

Conclusions: Differential expression of miRNA-21 in hESCs, hESC-, hF- and hA-VCMs is apparently unrelated to global functional maturity of hESC-CMs. High level of miRNA-21 expression during embryonic stage might confer survival advantages to developing myocytes.