INTERFERON STIMULATED LONG NONCODING RNA LINCARNACMPK2 FACILITATES NEUTROPHILS INTERFERON PRODUCTION BY TLR7/8 AGONIST IN SLE

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Background and aims Neutrophils are important source of high interferon in SLE, we aimed to identify Long noncoding RNAs (LncRNAs) that can be strongly induced by interferon and simultaneously show different expression in neutrophils of SLE and healthy controls. We also investigated how this LncRNA modulate neutrophils interferon production.

Methods RNA-seq was performed in two series of samples, interferon stimulated neutrophils samples and SLE versus healthy controls neutrophils samples. LncRNA-CMPK2 was screened out by cross-reference the two RNA-seq results. Neutrophils interferon production was measured by qPCR and ISRE report gene assay after LncRNA-CMPK2 was knocked down using antisense oligos electroporation.

Results SLE neutrophils produced more interferon when stimulated by TLR7/8 agonist R848 as compared to healthy controls. Neutrophils enhanced interferon production capacity after interferon prime. LncRNA-CMPK2 was an interferon stimulated LncRNA in neutrophils and had an expression level correlated with SLE disease activity. Knock down LncRNA-CMPK2 attenuated neutrophils interferon production.

Conclusions Interferon can augment neutrophils interferon production capacity in regenerative feedback. LncRNA-CMPK2 was an important interferon stimulated LncRNA and can facilitate neutrophils interferon production in SLE. Accommodate the expression of LncRNA-CMPK2 could probably supply a new thread of thought to SLE treatment.

DENDRITIC CELLS DISPLAY ABERRANT TOLL-LIKE RECEPTOR 7/9 RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease that causes multi-organ damages. Plasmacytoid dendritic cells (pDCs) are potent type I interferon (IFN) producers and myeloid dendritic cells (mDCs) are professional antigen presenting cells. Clinically, serum IFN-alpha (IFNα) level correlates with disease severity and mDCs from patients also display activated phenotypes. These observations suggested that different DCs subsets may mediate SLE pathogenesis. Therefore, the aim of this study was to evaluate whether pDCs and mDCs possessed aberrant properties that might mediate SLE progression.

Methods The properties of DCs from the murine lupus model New Zealand Black/White F1 (BWF1) were evaluated using flow cytometry, ELISA and qPCR.

Results Splenic pDCs abundance was similar before and after disease onset. The induction of CD40, CD80 and MHC II on pDCs upon Toll-like receptor (TLR) 7 or TLR9 stimulation and the level of IFN-alpha produced by pDCs in symptomatic and pre-symptomatic mice was also comparable. In contrast, splenic mDCs expanded in symptomatic mice. These mDCs decreased CD80 and MHC II expression but their ability in stimulating allogenic T cell proliferation was similar to mDCs from pre-symptomatic mice. On the other hand, TLR7 and TLR9 expressions in BWF1 mDCs were higher than mDCs from age- and sex-matched parental NZW controls. The amount of IL-10 and CXCL13 produced by mDCs from symptomatic mice upon TLR7 or TLR9 stimulation was also higher than its pre-symptomatic counterparts.

Conclusions Myeloid DCs displayed heightened TLR7 and TLR9 responses in SLE. More work is needed to further dissect how mDCs promote SLE pathogenesis.
Background and aims: There is no class I evidence available to treat children with lupus nephritis (LN). This study looked at our experience of management of LN and contribute to the existing world literature. In addition to treatment of LN, care is given to educate the family, manage lipids, BMI, restricting steroid use to 1 mg/kg/day at onset, give hydroxychloroquine to all and vaccinate if possible.

- To study the clinical profile and lab parameters of children at onset of nephritis.
- To see which of the two drugs cyclophosphamide (CYC) or mycophenolate mofetil (MMF) were more effective by studying the time to renal flare.
- To analyse the side effects and disease related damage in these children.

Methods: All children with lupus nephritis who attended the Paediatric Rheumatology clinic from Sept 2009 to Sept 2016 were included.

Results: 166 children with SLE, 67 had LN (40.3%); Male: Female=1:2.72. Median SLEDAI at nephritis onset: 18.

57 renal biopsies: Class I: 1, Class II: 5, Class III: 19, Class IV: 26, Class V: 6. MMF used to induce remission: 43 (64%), Cyclophosphamide (CYC) 19 (28%), Azathioprine: 5 (7%). 67% achieved complete remission during induction. 25% partial remission/flared after an initial response within induction period. Median time to response during induction therapy: 4 months (2–17 months). MMF was given to 82% and Azathioprine to 18% for maintenance. 36/62 (58%) never flared, 23/62 (37%) flared during induction therapy and 3/62 (5%) were in partial remission.

Conclusions: MMF and CYC were equally effective as induction agents and neither was superior to prevent renal flares. No factor: demographic, clinical or laboratory could predict renal flares. 58% were in renal remission, 33% on steroids.

The primary outcome measure, time to renal flare was statistically insignificant regardless of the induction agent used.

Abstract 124 Table 2 Outcome variables

Abstract 124 Table 1 Basic demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median duration of induction therapy</th>
<th>Median duration of follow up since nephritis diagnosis</th>
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<tr>
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<td>7 months (3–35)</td>
<td>48 months (3–159)</td>
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<tr>
<th>Median SLEDAI at onset of nephritis</th>
<th>Median SLEDAI at last follow up</th>
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<td>0 (0–43)</td>
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<th>At last follow up:</th>
<th>Complete remission</th>
<th>Active ds</th>
<th>Disease flare</th>
<th>Complete remission off DMARDs</th>
<th>Lost to follow up</th>
<th>Deaths</th>
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<td></td>
<td>58%</td>
<td>9%</td>
<td>7%</td>
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<th>Tuberculosis</th>
<th>Enteric fever</th>
<th>Viral infections</th>
<th>Herpes zoster</th>
<th>Dengue</th>
<th>CMV reactivation</th>
<th>Varicella</th>
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<tr>
<td></td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
<td>34% (21-67)</td>
<td>40% (9-23)</td>
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<td>13% (3-23)</td>
<td>4% (1-23)</td>
<td>4% (1-23)</td>
</tr>
</tbody>
</table>

Abstract 124 Table 2 Outcome variables

Abstract 124 Table 1 Basic demographics

- Median age at onset of SLE disease: 11 years (4-18 years).
- Median age at diagnosis of SLE disease: 11.75 years (4.5-18.16 years).
- Delay to diagnosis: 2.76 months (0.24-72).
- Median age at nephritis diagnosis: 12.2 years (4.5-24.5 years).
- Time to onset of nephritis (46 children had simultaneous onset of SLE disease and nephritis): 19 months (6.72-120 months).
- Median serum creatinine at onset of induction: 0.7 mg/dl (0.27-2.84).
- Median serum creatinine at onset of maintenance: 0.42 mg/dl (0.16-3).
- Urine spot protein/creatinine ratio at onset of induction: 1.96 (0.35-13.19).
- Urine spot protein/creatinine ratio at onset of maintenance: 1.3 gm (0.240-5.5).