Eosinophilic Research at the Cincinnati Center for Eosinophilic Disorders (CCED)

The Cincinnati Center for Eosinophilic Disorders (CCED) is a leader in research for these often-misunderstood conditions. Our research spans all states of therapeutic development. Developing new treatments and cures is an involved process that requires significant time and investment, especially during the fundamental stages of basic research and discovery validation, which are a major priority of the CCED. The CCED has a critical role in this process, working tirelessly on each stage, and has already had a key role in the development of therapeutic strategies for eosinophilic disorders such as eosinophilic esophagitis (EoE) and hypereosinophilic syndrome (HES).

**Stages of Therapeutic Development (**Level of CCED Involvement**)**

<table>
<thead>
<tr>
<th>Fundamental Research</th>
<th>Translational &amp; Preclinical Research</th>
<th>Drug Development</th>
<th>Clinical Trials (Phases I-III)</th>
<th>FDA Approval</th>
<th>Clinical Trials (Phase IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>***</td>
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</tr>
</tbody>
</table>

**Current* Pipeline of Diagnostic and Therapeutic CCED Research (**As of April 2017**)

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Target</th>
<th>CCED Research</th>
<th>Therapeutic Agent</th>
<th>CCED Clinical Trials</th>
<th>Phase of Development</th>
</tr>
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<tbody>
<tr>
<td><strong>Suppress inflammatory response</strong></td>
<td></td>
<td>1-3</td>
<td>Flovent</td>
<td>4,5 and Current Trial (enrollment closed)</td>
<td>Off-label clinical use</td>
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<tr>
<td>Systemic corticosteroids</td>
<td>Immune system</td>
<td></td>
<td></td>
<td></td>
<td>Off-label clinical use</td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>Local inflammation</td>
<td>1-3</td>
<td>Budesonide</td>
<td>III</td>
<td>Preclinical</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>CDH26</td>
<td>6,7</td>
<td>CDH26-Fc</td>
<td></td>
<td>Preclinical</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>NTRK1 (aka TRKA)</td>
<td></td>
<td></td>
<td></td>
<td>Preclinical</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>SPINK7 and A1AT</td>
<td>8</td>
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<td></td>
<td>Preclinical</td>
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</tbody>
</table>

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### Current* Pipeline of Diagnostic and Therapeutic CCED Research (continued)

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Target</th>
<th>CCED Research</th>
<th>Therapeutic Agent</th>
<th>CCED Clinical Trials</th>
<th>Phase of Development</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Block eosinophil recruitment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Chemokine inhibition</td>
<td>CCR3</td>
<td>9-36</td>
<td></td>
<td>Bertilimumab</td>
<td>II</td>
</tr>
<tr>
<td>Chemokine inhibition</td>
<td>CCL11 (eotaxin-1)</td>
<td>9,10,12,14,17,20,22,25-27,30,31,33,35-77</td>
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<tr>
<td>Cytokine inhibition</td>
<td>IL-13</td>
<td>1,3,17,18,20,27,29,30,33,34,56,59,60,62,66,70,75,78-112</td>
<td>QAX576</td>
<td>Current Trial (ongoing)</td>
<td>III</td>
</tr>
<tr>
<td>Cytokine receptor inhibition</td>
<td>IL-13R</td>
<td>30,79,81,82,91,103,105,107,108</td>
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<td>RPC4046</td>
<td>III</td>
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<tr>
<td>Cytokine receptor inhibition</td>
<td>IL-4R</td>
<td>30,34,75,78-</td>
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<td>Dupilumab</td>
<td>II</td>
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<tr>
<td>Anti-inflammatory</td>
<td>TGF-β</td>
<td>30,72,106,115</td>
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<td>Lorsartan</td>
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<tr>
<td><strong>Adhesion molecule inhibition</strong></td>
<td>Periostin</td>
<td>116</td>
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<td>Preclinical</td>
</tr>
<tr>
<td>Chemokine inhibition</td>
<td>CCL26 (eotaxin-3)</td>
<td>1,3,24,29,80,83,104,117-119</td>
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<td>Epigenome modifiers</td>
<td>Epigenome</td>
<td>83</td>
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<td>Preclinical</td>
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<tr>
<td><strong>Inhibit eosinophil activation</strong></td>
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<tr>
<td>Cytokine inhibition</td>
<td>TSLP</td>
<td>120,121</td>
<td>AMG 157</td>
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<td>II</td>
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<tr>
<td>Cytokine inhibition</td>
<td>IL-33</td>
<td>Pre-publication</td>
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<td>Preclinical</td>
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<tr>
<td><strong>Inhibit eosinophil survival</strong></td>
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<tr>
<td>Cytokine inhibition</td>
<td>IL-5</td>
<td>10,14,16,18,25,28,29,32-34,41,47,49,50,52,53,56,58-64,66,71,73,75,76,80,105,112,122-144</td>
<td>Mepolizumab</td>
<td>28,32,130,139</td>
<td>FDA-approved for eosinophil asthma</td>
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<tr>
<td>Eosinophil depletion</td>
<td>IL-5R-α</td>
<td>126,138,145,146</td>
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<td>Benralizumab</td>
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<tr>
<td>Activation of inhibitory receptor</td>
<td>Siglec-8</td>
<td>126,138,145,146</td>
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<td>Preclinical</td>
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<tr>
<td>Activation of inhibitory receptor</td>
<td>PIRB</td>
<td>31,147</td>
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<td><strong>Modulate epithelial barrier</strong></td>
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<tr>
<td>Cysteine protease modulation</td>
<td>CAPN14</td>
<td>148</td>
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<td>Preclinical</td>
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<tr>
<td>Adhesion molecule inhibition</td>
<td>CDH26</td>
<td>6,7</td>
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<td>Fundamental</td>
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<td>Barrier integrity modulation</td>
<td>Barrier function</td>
<td>107,149</td>
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<td>Fundamental</td>
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<td><strong>Molecular diagnostics</strong></td>
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<td>Gene expression</td>
<td>Eosinophilic Esophagitis</td>
<td>1,108,110,150-152</td>
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<td>Clinical validation</td>
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</table>
References


Herbert DR, Orekov T, Perkins C, Rothenberg ME, Finkelman FD. IL-4R alpha expression by bone marrow-derived cells is necessary and sufficient for host protection against acute schistosomiasis. *Journal of immunology*. 2008;180(7):4948-4955.


