<table>
<thead>
<tr>
<th>PRRs and signalling adaptors in IECs</th>
<th>In vivo effect on IECs</th>
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<tbody>
<tr>
<td><strong>TLRs</strong></td>
<td></td>
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<tr>
<td>TLR1&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>ND</td>
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</tbody>
</table>
| TLR2<sup>3–7</sup>                 | • Protects IECs from injury<sup>1</sup>  
|                                    | • Enhances M cell transport<sup>4</sup>  
|                                    | • Promotes gap junction communication<sup>6</sup>  
|                                    | • Increased TFF3 production<sup>7</sup>  
|                                    | • Promotes tight junction integrity<sup>6</sup>  |
| TLR3<sup>8,9</sup>                 | • Promotes IEC IL-15 production and IEL cytotoxicity<sup>8,9</sup>  |
| TLR4<sup>10–14</sup>               | • Protects IECs from injury<sup>3</sup>  
|                                    | • Promotes tumour development and growth<sup>12,14</sup>  
|                                    | • Increases prostaglandin production<sup>12</sup>  
|                                    | • Promotes necrotizing enterocolitis (in neonates)<sup>15,16</sup>  
|                                    | • Increases serum amyloid A production<sup>17</sup>  
|                                    | • Promotes tight junction integrity<sup>5</sup>  |
| TLR5<sup>18–23</sup>               | • Promotes chemokine and cytokine production<sup>18</sup>  
|                                    | • Protects against apoptosis<sup>19,21</sup>  
|                                    | • Limits IL-1β mediated inflammation<sup>22</sup>  
|                                    | • Prevents bacterial overgrowth<sup>16</sup>  |
| TLR9<sup>10,24–28</sup>            | • Inhibits NF-κB activation and tolerizes subsequent TLR signalling<sup>25</sup>  
|                                    | • Protects against necrotizing enterocolitis (in neonates)<sup>18</sup>  
|                                    | • Promotes Paneth cell degranulation<sup>24</sup>  
|                                    | • Promotes AMP production<sup>24,28</sup>  
|                                    | • Protects IECs from injury<sup>16,25,27,28</sup>  |
| TLR10<sup>29</sup>                 | • ND                  |
| TLR11<sup>30–32</sup>              | • Prevents epithelial entry and dissemination of pathogenic *Salmonella* species<sup>31,32</sup>  |
| TRIF<sup>33</sup>                  | • Promotes IEC apoptosis<sup>33</sup>  |
| **MYD88**<sup>34–41</sup>         | • Protects IECs from injury<sup>3,16</sup>  
|                                    | • Promotes AMP secretion<sup>37,41,42</sup>  
|                                    | • Increases mucin production<sup>42</sup>  
|                                    | • Promotes prostaglandin production<sup>38</sup>  
|                                    | • Protects IECs from injury<sup>16,25,27,28</sup>  |
| **TAK1**<sup>45–48</sup>          | • Prevents IEC apoptosis<sup>45–48</sup>  
|                                    | • Promotes IEC proliferation<sup>45,48</sup>  
|                                    | • Promotes AMP production<sup>47</sup>  
|                                    | • Limits accumulation of ROS<sup>46,47</sup>  |
| **TAB1–TAB2**<sup>47</sup>        | • Limits accumulation of ROS<sup>47</sup>  |
| **RLRs**                           |                       |
| RIG-I<sup>49,50</sup>              | • ND                  |
| MDA5<sup>50</sup>                  | • Promotes interferon production<sup>50</sup>  |
| MAVS<sup>50,51</sup>               | • Protects IECs from injury<sup>51</sup>  |
| **NLRs**                           |                       |
| NOD1<sup>52–54</sup>               | • Protects IECs from injury<sup>3,16,18</sup>  
|                                    | • Inhibits tumour development<sup>53</sup>  
|                                    | • Induces intestinal lymphoid tissue formation<sup>52</sup>  
|                                    | • Recruits autophagy proteins<sup>54</sup>  |
| NOD2<sup>54–59</sup>               | • Recruits autophagy proteins<sup>54</sup>  
|                                    | • Promotes AMP production<sup>57,58</sup>  
|                                    | • Promotes ROS production<sup>59</sup>  |
| NLRP3<sup>60–66</sup>              | • Inhibits tumour development<sup>61,64</sup>  
|                                    | • Promotes or limits colitis (depending on circumstances)<sup>61–63,65</sup>  
|                                    | • Promotes AMP production<sup>66</sup>  
|                                    | • Regulates commensal microbial composition<sup>66</sup>  |
| NLRP6<sup>65,67–69</sup>           | • Protects IECs from injury<sup>67,68</sup>  
|                                    | • Promotes colonic wound healing<sup>68</sup>  
|                                    | • Inhibits tumour development<sup>67,68</sup>  
|                                    | • Regulates commensal microbial composition<sup>65</sup>  
|                                    | • Inhibits NF-κB and MAP kinase responses to bacterial infection<sup>69</sup>  |
**NLRs (cont.)**

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<thead>
<tr>
<th>NLR</th>
<th>Function</th>
<th>Reference</th>
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</table>
| NLRC4 | *Inhibits tumour development and proliferation*<sup>70</sup>  
*Protects IECs from injury*<sup>71</sup>  
*Protects against *Salmonella* infection*<sup>71</sup> |  |
| NLRP12 | *Limits inflammatory response to injury*<sup>72–74</sup>  
*Limits tissue repair following injury*<sup>72</sup>  
*Inhibits tumour formation and growth*<sup>73–74</sup> |  |
| Caspase 1 | *Protects IECs from injury*<sup>61,63,72</sup>  
*Inhibits tumour development*<sup>61,72</sup> |  |
| Caspase 12 | *Inhibits tumoral repair*<sup>72</sup>  
*Inhibits tumour development*<sup>72</sup> |  |
| **PRR signalling pathways in IECs** |  |
| NF-κB Signalling | IKK1 | *Inhibits IEC apoptosis*<sup>76,77</sup>  
*Promotes AMP production*<sup>76,77</sup>  
*Protects IECs from injury*<sup>78</sup>  
*Promotes tumour development*<sup>79,80</sup> |  |
| NEMO |  |  |
| RelA |  |  |
| MAP Kinase Signalling | p38α | *Promotes goblet cell differentiation*<sup>83</sup>  
*Inhibits proliferation*<sup>83</sup> |  |
| **IEC negative regulators of PRR signalling** |  |
| SIGIRR | *Inhibits TLR signalling*<sup>84,85</sup>  
*Limits proliferation*<sup>85</sup>  
*Protects IECs from injury*<sup>85</sup>  
*Inhibits tumour development and progression*<sup>85</sup> |  |
| A20 | *Inhibits apoptosis*<sup>86,90–92</sup>  
*Protects IECs from injury*<sup>86,90–92</sup>  
*Inhibits NF-κB activation by PRRs and cytokine receptor*<sup>86,87,89,90</sup> |  |
| MKP1 |  | ND |  |
| miR-146a |  | *Inhibits TLR signalling during the neonatal period*<sup>95</sup> |  |

Bold font designates evidence for IEC-specific role based on targeted deletion or transgenic expression in murine models.

* Indicates expression only in mice, and not in humans.

AMP, antimicrobial peptide; APRIL, a proliferation-inducing ligand; BAFF, B cell activating factor; IEC, intestinal epithelial cell; IEL, intraepithelial lymphocyte; ND, not determine; pIgR, polymeric immunoglobulin receptor; ROS, reactive oxygen species; TFF3, trefoil factor 3; TLR, toll-like receptor;

SUPPLEMENTARY INFORMATION


