**Table 2:** Mechanisms of action of Polyphosphazene adjuvants: Non-specific immune responses to polyphosphazene adjuvants injected in the absence of antigen

| Animal species | Adjuvant(s) | Route of administration | Immune responses | References |
|----------------|-------------|-------------------------|------------------|------------|
| Mice           | PCEP        | IM                      | ↑ IFN-γ, ↑ inflammasome activation | Awate 2012 |
|                |             | IM                      | Dose dependent, pro-IL-1 induction leading to ↑IL-1 /IL-18, ↑ CD8+ T cell response | Awate 2014 (a) |
|                |             | IM                      | ↑ T cell recruitment to dLNs (CD4/CD8+), ↑ total leukocyte recruitment @ SOI | Awate 2014 (b) |
|                | PCEP+IDR+Poly: I:C “P-I-P” | IN                      | ↑ mRNA and protein expression cyto/chemokines in lung milieu (CXCL10, CCL2, CCL3, CXCL2, CXCL1), ↑ upregulation of TNF-α, IL-1 , and IL-6, ↑ immune cell infiltration observed in lungs without causing toxicity, P-I-P less effective when given further away from challenge- survival rate ↓ | Martinez 2016 |
|                |             | IN                      | 100% survival rate upon virulent PVM-15 challenge, ↑ protein concentrations of TNF-α in BALF, ↑ IL-17E in lungs, ↑ AM in response to PIP treatment, innate protection observed to last up to 1 wk | Martinez 2019 |
| Pigs   | PCEP    | ID | ↑Th2 response (IL-6/IL-13), early onset of immune response |
|--------|---------|----|-----------------------------------------------------------|
|        |         | ID | ↑ Th2 cytokine response at SOI and dLNs, induce acute inflammation, local inflammation at SOI, trigger innate immunity |
|        |         |    | Magiri 2016                                               |
| Chicken| PCPP+CpG-ODN/PCPP+CpG-ODN | In ovo (SC) | No AEs or poor hatchability in embryos, effective against *E. coli* challenge, significant ↓ in mortality in embryos immunized with PCPP/PCEP+CpG-ODN compared to control; PCEP alone also provided modest protection |
|        |         |    | Taghavi 2009                                              |

**Abbreviation** | **Description**
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AEs | Adverse reactions/events
PCEP | Poly[di(sodiumcarboxylatoethylphenoxy)phosphazene]
PCPP | Poly [di(carboxylatophenoxy)phosphazene]
SOI | Site of injection
| Abbreviation | Description |
|--------------|-------------|
| IN           | Intranasal  |
| IM           | Intramuscular |
| ID           | Intradermal |
| SC           | Subcutaneous |
| MP           | Micro particle |
| BALF         | Bronchoalveolar lavage fluid |
| dLNs         | Draining lymph nodes |
| IDR          | Innate defense regulatory peptides |
| MatAbs       | Maternal Antibodies |
| PVM-15       | Pneumonia virus of mice strain 15 |