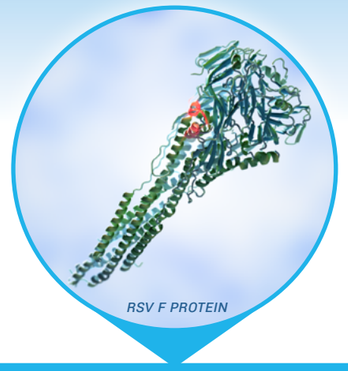
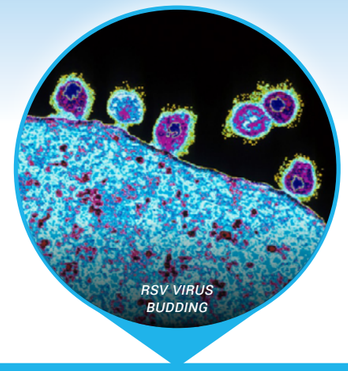
NOVAVAX
Creating Tomorrow's Vaccines Today

A History of RSV Vaccine Development: 60 Years. One Goal.





ANNUALLY IN THE **US**, IN **ADULTS 65** AND **OLDER**

RSV INFECTIONS: **2,400,000**

MEDICAL INTERVENTIONS: **900,000**

DEATHS: **14,000**

1950s/60s/70s

1956
RSV is first isolated from a group of chimpanzees

1957
Virus identified in humans[1]

1963
Robert Chanock isolates and characterizes the virus

1966-69
Formalin-inactivated RSV was tested in infants and young children[2]

- The vaccine stimulated moderately high levels of serum antibodies but failed to induce resistance to infection
- Some vaccinated infants developed a more serious disease when later infected with the disease
- 2 infants died following infection with RSV

1970s
Sf insect cells first isolated from the ovaries of the fall armyworm (*Spodoptera frugiperda*)

1980s/EARLY 1990s

Early 1980s
Novavax senior scientist and VP of Vaccine Development, Gale Smith, Ph. D., discovered the "Sf9" insect cell line could grow in apparent perpetuity in a special culture medium and can produce recombinant proteins upon infection with a baculovirus, a virus that infects only insects

1980s
Ribavirin, which decreases replication *in vitro*, shown to have no clinical utility in trials

1985-86
MedImmune develops monoclonal antibody; Palivizumab

Early 1990s
Wyeth tests a purified fusion (F) protein vaccine in children with cystic fibrosis[3]

- While protection against RSV infection was not observed, there was a significant reduction in lower respiratory tract illnesses, antibiotic courses and days ill

1990s/EARLY 2000s

1994-97
MedImmune takes Palivizumab into clinical trials

1998
Palivizumab (Synagis; **MedImmune**) approved to treat lung disease and respiratory infections that result from RSV infection in premature infants

Early 2000s
Wyeth tests a subunit RSV vaccine with purified F protein via maternal immunization[4]

Wyeth tests a third-generation purified fusion protein vaccine in children with cystic fibrosis[5]

2007
Sanofi tests a subunit vaccine containing the RSV fusion (F), attachment (G) and matrix (M) proteins in the elderly[6]

2000s/2010s

2009
Initial **Novavax** preclinical data

2010-2013
Novavax Phase 1 clinical trials with Recombinant RSV F Vaccine[7]

- Vaccine induced anti-F IgG and palivizumab-competing antibody titers at levels associated with decreased risk of hospitalization

2013
Novavax announces positive data from Phase 2 trial of RSV F Vaccine in women of childbearing age

- Significant anti-F IgG antibody response across all vaccine doses

Novavax initiates Phase 2 dose-confirmatory trial of RSV F Vaccine in women of childbearing age

2013-2014
GSK Phase 1 clinical trial of recombinant RSV vaccine in healthy men[8]

2014

Novavax announces positive data from Phase 2 dose-confirmatory trial of RSV F Vaccine in women of childbearing age

- Highest immune responses observed with a single dose of vaccine combined with aluminum phosphate adjuvant
- High levels of antibodies developed within 14 days after immunization and persisted over the 91-day observation period

MedImmune in Phase 1 with RSV sF antigen vaccine in older adults[9]

Novavax initiates Phase 2 clinical trial of RSV F Vaccine for protection of infants via maternal immunization

Novavax initiates Phase 2 clinical trial of RSV Vaccine in older adults (ages 60+)

Novavax granted Fast Track Designation by U.S. FDA for RSV F Vaccine for protection of infants via maternal immunization

ONGOING

2011-Ongoing
MedImmune/NIH/NIAID Phase 1 with recombinant live-attenuated vaccine in adults, children and infants[10]

2013-Ongoing
NIH/NIAID testing recombinant live-attenuated vaccines in Phase 1 with infants and children[11]

ReiThera Srl in Phase 1 with vaccine based on the RSV viral proteins F, N and M2-1 encoded by Simian Adenovirus (PanAd3-RSV) and Modified Vaccinia Virus Ankara (MVA-RSV) in healthy and older adults[12]

2014-Ongoing
Novartis in Phase 1 with RSV F subunit vaccine in healthy adults[13]

2015

GSK begins Phase 2 trial of recombinant RSV vaccine in healthy women[14]

Bavarian Nordic developing recombinant MVA-BN vaccine encoding two RSV surface proteins[15]

- Vaccine candidate induced protective immune response in a preclinical model, without inducing inflammation in the lungs as measured by induction of eosinophils

ImmunoVaccine in Phase 1 with SHe Antigen vaccine for older adults[16]

Crucell Holland BV in Phase 1 with human adenovirus-vectored vaccine in healthy adults[17]

Novavax announces first ever RSV vaccine to demonstrate efficacy in a prospective controlled clinical trial in any population

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