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RESEARCH ARTICLE

RECOMBINANT PROBIOTIC *SACCHAROMYCES CEREVISIAE VAR. BOULARDII* AS BIO-MEDICINE: A REVIEW

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ABSTRACT

Strategies have been developing to treat and prevent physiological and metabolic disorders by use of genetically modified microorganisms as a nutritional supplement. The present review focuses on the recombinant probiotics of *Saccharomyces cerevisiae var. boulardii*, which plays a major role in human gastric conditions like high temperature, low pH, mixtures of organic acids, maximum bile, high concentrations of gastric juices, and anaerobic conditions. Along with this tolerance, recombinant probiotics can absorb zinc sulfate, enhance vitamin B6 productivity, convert CIN into COU, and resist 5-fluoroorotic acid, uracil, and uridine by the expression of desired enzymes, whereas in the wild type it is not observed. Probiotic *Saccharomyces cerevisiae*, in addition to its probiotic activity, has been showing a few therapeutic applications in humans, like enhanced antimicrobial and prophylactic activity by point mutations and by the expression of serum albumin, insulin, transferrin, hirudin, urate oxidase enzymes, and GM-CSF. After genetic manipulation in the probiotic *Saccharomyces cerevisiae*, it enhanced immunological effects in the host for the expressed antigens like β-lactamase, *S. aureus* nuclease A, TSST-I, the A-chain of Shiga-like toxin, heat-labile enterotoxin, cholera toxin-B, ASPs, Bloom and Werner's syndrome, HBsAg, HCV, PEDV, cervical cancer, CD4+, and CD8+. Similar findings were noted with recombinant probiotic *Saccharomyces cerevisiae* in veterinary applications like phytate degradation, bovine interferon, growth hormone expression, and immunization to IBD, porcine pleuropneumonia, PPV, ETEC antigens, etc. In the fishery field, recombinant Saccharomyces cerevisiae is used as a probiotic for nutritional supplements, for the expression of growth hormone, for immunization to *Vibrio harveyi*, and for pancreatic necrosis. Slight modifications in the gene sequence and by expression of specific genes in beneficial organisms like the probiotic *Saccharomyces cerevisiae* may result in reduction of metabolic disorders in the living forms.

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INTRODUCTION

Genera of *Saccharomyces, Kluyveromyces* and some other yeast strains are animal and environmentally friendly microorganisms (Kopp Hoolihan, 2001). These strains have been applied to nutritional, clinical, therapeutic and industrial processes. These are highly specialized microorganisms as they utilize ecological niches for their potential growth (Querol *et al*., 2003). For adapting to these conditions, microorganisms were exposed to traditional (mutations) and applied genetic modifications (recombinant DNA technology) (Primrose, 1986) to develop safe mutant for several applications. Now a days, these recombinant microorganisms are administered orally for several medical applications as biodrug therapy (Alric *et al*., 2000; Blanquet *et al*., 2001; Corthier *et al*., 1999). Xenobiotics like pesticides, procarcinogens, and chemical additives were detoxified by expressing cytochrome p450 enzyme (Fahl *et al*., 1999; Srinivas *et al*., 2021). Another important property of recombinant microorganisms is activation of prodrug into drug in the digestive tract directly (Blanquet *et al*., 2001), corrects metabolic disorders like gastric enzymes deficiency (Drouault *et al*., 2002) and organ failure (kidney) (Prakash *et al*., 2000). Genetically modified microorganisms, such as bacteria and yeast act as a new delivery vehicle to the gastrointestinal tract of human and animals for development of innovative drugs (Blanquet *et al*., 2001). Among these organisms *Saccharomyces cerevisiae var. boulardii* is selected (Corthier *et al*., 1999; Canganella *et al*., 1997), because heterologous genes can be functionally expressed especially in the eukaryotic environment (Corthier *et al*., 1999). *S. cerevisiae*, has also been used as a probiotic for human (Canganella *et al*., 1997) applications, as it is "generally recognized as safe", eukaryotic, and it tolerates digestive secretions (Blanquet *et al*., 2003). Recombinant yeast strains show highest viability in human upper gastrointestinal tract and viability decreases 1% for 24hrs in the large intestine (Blehaut *et al*., 1989). An attractive and alternative commonly used route of vaccination is oral vaccination, because yeast has potential live delivery system and it is inherently non -pathogen (Yu *et al*., 1996; Scott., D. *et al*., 1998; Andressa Ardiani *et al*., 2010). *Saccharomyces* has the ability to perform eukaryotic post translational modifications and express a wide range of therapeutic proteins and growth hormones in humans (Lauren., H. *et al*., 2015), veterinary and fishery field (Ellis *et al*., 1995).

APPLICATIONS OF RECOMBINANT PROBIOTIC *SACCHAROMYCES CEREVISIAE VAR. BOULARDII:* Revolutionary impact in the area of human healthcare has been made by the development of recombinant DNA (rDNA) technology by production of large-scale rDNA products. Now a days, numerous rDNA products like hormones of therapeutic interest, haemopoietic growth factors, blood coagulation products, thrombolytic agents, anticoagulants, interferons, and therapeutic enzymes are being produced for human applications (Bhopale *et al*., 2005). To reduce economical values in scale up production, probiotic *S. cerevisiae* has to utilize economically cheaper substrates such as agro waste. Wild *S. cerevisiae* can't utilize cellulolytic medium, where as recombinant strain can utilize by expressing cellulose degrading enzymes such as endoglucanase, exoglycanase and β-glucosidase (Dae Kyun Chung *et al*., 1997).

Human Gastrointestinal Applications: Probiotic characteristics of free-living *Saccharomyces cerevisiae* is that it must adapt to stress conditions like temperature, (Daquinag *et al*., 2007) mixture of organic acids, pH, bile (Hassan Hamedi *et al*., 2013), high concentration of digestive secretions like trypsin, amylase, pepsin and toxic ions (Trabalzini *et al*., 2003; Platara *et al*., 2006, Srinivas *et al*., 2017). Viability of mutant or recombinant *Saccharomyces boulardii* is higher than wild, when cultured in anaerobic gastric environment (Lauren., H. *et al*., 2015). Surveillance of wild and recombinant *Saccharomyces boulardii* at pH 3.0 and 0.3% bile concentration is 4.7; 7.7 *log* CFU and 5.0; 8.3 *logs* CFU respectively. Recombinants can also tolerate 5% bile and alkaline pH (Abdel *et al*., 2007). 100mM acetic acid at pH 4.5 creates toxic environment to wild type *Saccharomyces cerevisiae,* but it favors the viability of recombinants, 0.4-1.8% Zinc Sulphate absorption was observed in wild type and 2.2-3.5% in recombinant (Nuno *et al*., 2010). Vitamin B6 productivity of wild type *Saccharomyces boulardii* is 0.8mg/g biomass but in recombinant it is 1.13mg/g (Ahmed Nageb Sharaf *et al*., 2009).

Survival rate in digestive secretions of Cytochrome p450 73A1 expressing recombinant *Saccharomyces cerevisiae* is 95.6% ± 10.1% and (Klein *et al*., 1993) for wild type is 36% ± 0.31% (Pecquet *et al*., 1991; Yu *et al*., 1996) after 4hrs of digestion. Bioconversion rate of *trans*-cinnamic acid (CIN) into *p*-coumaric acid (COU) 35.9% ± 2.7%, 41.0% ± 5.8%, 8.9% ± 1.6%, 13.8% ± 3.3%, 11.8% ± 3.4%, 6.5% ± 1.0% and too weak in colonic conditions, small intestine, stomach, duodenum, jejunum, ileum and large intestine respectively and 15% of CIN break down was observed with (is it a construct) plant cytochrome p450 73A1 expressing *Saccharomyces cerevisiae* (Blanquet *et al*., 2003; Garrait *et al*., 2007). Wild type *Saccharomyces boulardii* is sensitive to 5-Fluoroorotic acid, uracil and uridine due to the presence of URA3 gene (Umezu *et al*., 1971), but in mutant type it is resistant to 5-Fluoroorotic acid and grows well in the presence of uracil and uridine as it acts as a potential host for the production of pharmaceutical products in intestinal lumen (Arino., J. *et al*., 2010) (Table 1 & Fig. 2).

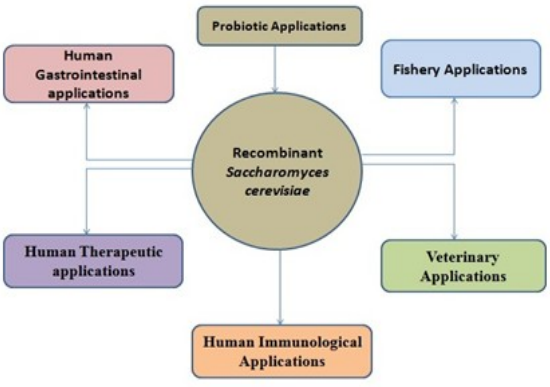

Fig. 1. Applications of recombinant probiotic *Saccharomyces cerevisiae*

Human Therapeutic Applications: Both therapeutic and biomanufacturing applications with animal free recombinant proteins offer effective and safe substitute to the tissue or serum derived products (Christopher *et al*., 2010). Antimicrobial activity of *Saccharomyces boulardii* on *B. cereus* is 8mm, *S. aureus* is 5mm and it is absent in case of *E. coli* and *P. aeruginosa* (Kuhle *et al*., 2005), but mutant or recombinant shows enhanced antimicrobial activity on *P. aeruginosa, B. cereus* and *S. aureus* as 9mm, 11mm and 10mm respectively (Nuno *et al*., 2010; Lauren., H. *et al*., 2015). In addition to these, an important biopharmaceuticals like human serum albumin recombination pathways were reviewed by Jens., N. 2013. Various approaches have been developed for recombinant biologically active human insulin expression in *Saccharomyces cerevisiae* pYT7810 vector and ADH1 promoter (Stepien, 1983). Recombinant *Saccharomyces boulardii* plays a novel therapeutic prophylactic role in intestinal neoplasia by inhibiting its epidermal growth factor receptor (EGFR) and other tyrosine kinase signaling receptors (Xinhua chen *et al*., 2009).

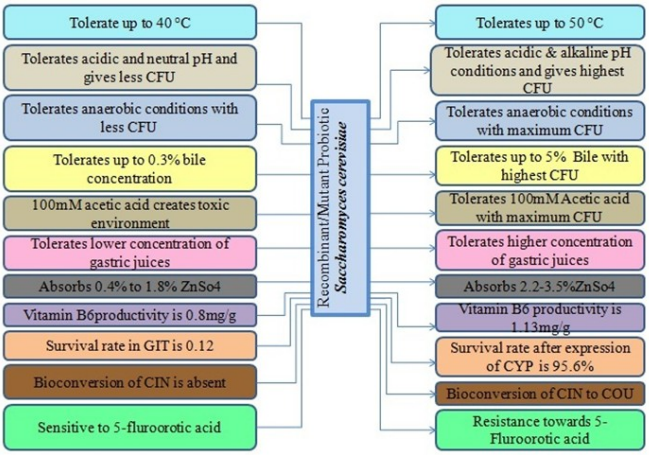

Fig. 2. Human Gastrointestinal Applications of recombinant probiotic *Saccharomyces cerevisiae*

A therapeutically and diagnostically important enzyme Urate oxidase coding gene from *Aspergillus flavus* was cloned in pPICZαA vector and expressed in *Saccharomyces cerevisiae* for the treatment of hyperuricemia conditions (Ramin Fazel *et al*., 2014). Increased production of recombinant human albumin (rHA) by random mutations in ATPase cycle of Kar2p regulating genes *SIL1*, *LHS1*, *JEM1*, and *SCJ1* was observed (Payne *et al*., 2008). Hirudin, a potent thrombin inhibitor coding gene of leech *Hirudo medicinalis* under the control of a glyceraldehyde- 3-phosphate dehydrogenase (GAP) promoter (Jutta., H. *et al*., 1994) and Human, (h) murine (m) granulocyte-macrophage colony stimulating factors (GM-CSF) were expressed in *Saccharomyces cerevisiae* by pHGM1 vector and α-factor for large scale production (Miyajima *et al*., 1986) (Table 2 & Fig. 3).

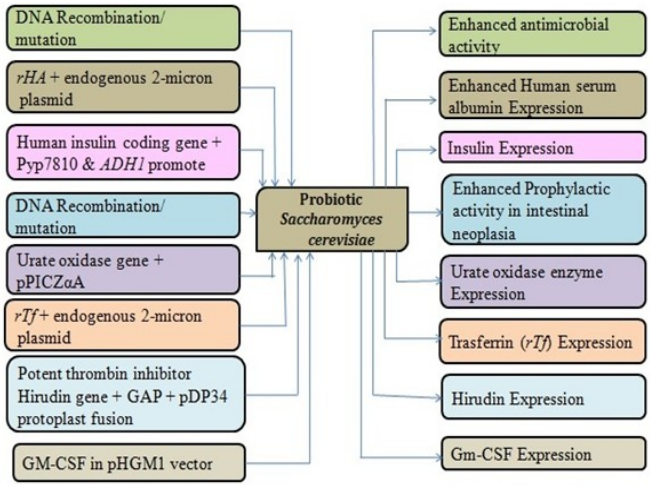

Fig. 3. Human Therapeutic Applications of recombinant probiotic *Saccharomyces cerevisiae*

Human Immunological Applications: The goal of therapeutic vaccines is to develop and activate patient's immune system as dynamically and enthusiastically and also offers potential prevention for disease reappearance. *Saccharomyces cerevisiae* based therapeutic vaccines were administrated in combination with cytotoxic drugs to achieve a greater clinical response in the host (Lauren., H. *et al*., 2015). Currently prokaryotic proteins like β-lactamase in pBR325 (Rainer., R. *et al*., 1981), *Staphylococcus aureus nuclease A* in Yep51vector, GAL 10 promoter (Pines., O. *et al*., 1991), Toxic Shock Syndrome Toxin-I (TSST-I) in pR600 vector (Robert *et al*., 1994), Shiga-like toxin I A-chain in pRSATT, GAL 1 promoter (Schonberger *et al*., 1991; Paul., L. P. *et al*., 2005), heat labile enterotoxin beta subunit in pYEGLTB vector, GAL1 promoter (Deresiewicz *et al*., 1992; Lim *et al*., 2009) and Cholera toxin B in pGETM-T (Mohsen., A. *et al*., 2005; Bita Bakhshi *et al*., 2014) were expressed in *Saccharomyces cerevisiae.* Infective third-stage larvae (L3) of the hookworm recombinant Ancylostoma-secreted proteins (ASPs), Ancylostoma ceylanicum Ay–ASP-1 and Ay-ASP- 2 were cloned into pPICZαA and expressed in *Saccharomyces cerevisiae* for the prevention of hookworm infections (Gaddam., N.G. *et al*., 2004). SGS1gene of *Saccharomyces cerevisiae* (Yu *et al*., 1996; Abdel *et al*., 2007) was cloned into pYC12 vector and expressed in *S. pombe* as well as *Saccharomyces cerevisiae* for immunization (Scott., D. *et al*., 1998). In this construct, two major hydrophobic fragments of hepatitis virus have been expressed on the surface of *S. cerevisiae* as a single fusion protein (Schreuder *et al*., 1996). Genetically modified HCV core E1E2 protein was cloned in pPICZαA and expressed in *Pichia pastoris* and *S. cerevisiae* for prevention of Hepatitis C Viral infection (Mehdi Fazlalipour *et al*., 2014).

Korean strain of Porcine Epidemic Diarrhea Virus (PEDV) neutralizing epitope of spike protein encoding gene K-COE was engineered with a signal peptide of rice amylase 1A (*Ramyl 1A*) and fused with carboxyterminal (320 amino acid residues) of alpha-agglutinin, and cloned into pYEGPD vector for covalently anchoring on cell wall of *S. cerevisiae* with the help of glyceraldehyde-3-phosphate dehydrogenase (*dma*) promoter (Seung., M.P. *et al*., 2007) to enhance immune response against PEDV. HPV 16 L1 coding sequence was cloned into YEGalpha-HIR525 vector and expressed in *Saccharomyces cerevisiae,* gene expression was regulated by GAL 1, HXT 5, PGK1, SML 1 and SSA 3 promoters (Walid., O. *et al*., 2005; Woo *et al*., 2008). For immunization of cervical cancer, viral specific engineered tumour or viral antigens $CD4^+$, $CD8^+$ were cloned in pGI-162 and expressed in *Saccharomyces cerevisiae* for an ideal therapeutic approach to reduce the risk of the disease (Andressa Ardiani *et al*., 2010; Elizabeth *et al*., 2008) (Table 3 & Fig. 4).

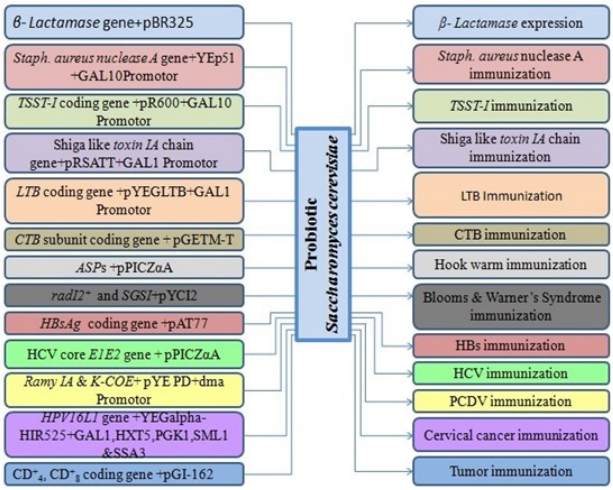

Fig. 4. Human Immunological Applications of recombinant probiotic *Saccharomyces cerevisiae*

Veterinary Applications: Phytate degradation was observed up to 60% in early gastric phase by sub cloning of PhyA gene of *Aspergillus niger* in pYES2 vector expressed in *Saccharomyces cerevisiae* but no phytate degradation was observed in wild type (Haraldsson *et al*., 2005; Hassan Hamedi *et al*., 2013).

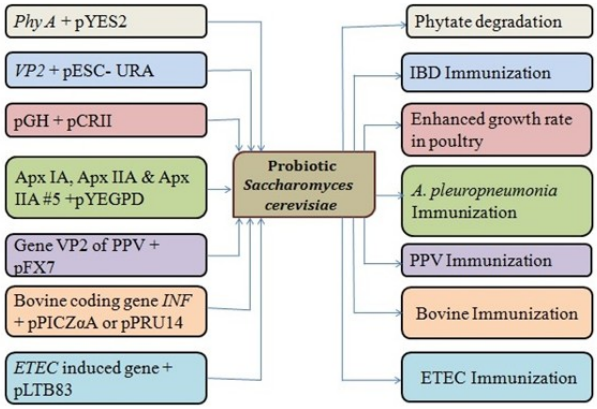

Fig. 5. Veterinary Applications of recombinant probiotic *Saccharomyces cerevisiae*

An immunosuppressive disease Infectious bursal disease (IBD) in chicks was caused by *Birna virus*, which is responsible for higher economic loss in poultry industry worldwide. A major structural protein VP2 has cloned in pESC-URA vector and expressed in *S. cerevisiae* to induce immune response against IBD (Sohini Dey *et al*., 2009). Porcine pleuropneumonia in pigs was caused by *Actinobacillus pleuropneumoniae* and it induces significant economic

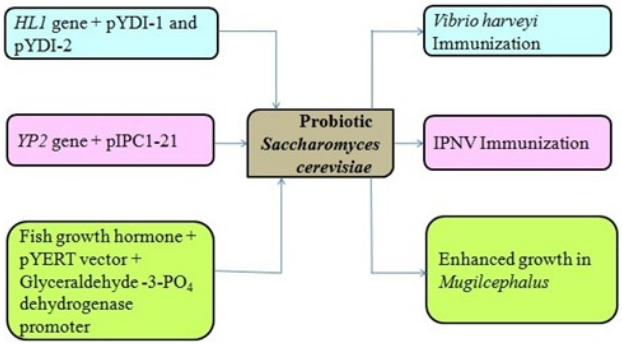

Fig. 6. Fishery Applications of recombinant probiotic *Saccharomyces cerevisiae*

loss worldwide, so responsible genes ApxIA, ApxIIA and ApxIIA#5 were cloned in pYEGPD for surface display on *S. cerevisiae* to induce immune response in mice and pigs, against *A. pleuropneumoniae* (Min Kyoung Shin *et al*., 2013). Porcine parvovirus (PPV) is a causative agent of serious reproductive diseases of swine and death of piglets, capsid protein VP2 of PPV coding gene sequence of viral nucleic acid is cloned in to pFX7 and expressed in *Saccharomyces cerevisiae* to control *Porcine parvovirus* disease in swine and piglets (Paulius., L. T. *et al*., 2014). In piglets Enerotoxigenic *Escherichio coli* (ETEC) results in large economic loss worldwide by causing inflammation, diarrhoea and intestinal damage, β-galactomanan (βGM) and *Saccharomyces cerevisiae var. boulardii* show similar protective role against ETEC. mRNA of ETEC-induced gene was cloned in to pLTB83 vector and expressed (Roger., B. *et al*., 2012; Rezaee., M.A. *et al*., 2005). Interferons of bovine and swine origin can be used as therapeutic drugs for the treatment of bacterial and viral infections in animals when the interferon coding gene was cloned in to pPICZαA or pPRU14 vector and expressed in *Saccharomyces cerevisiae* (Anastasia Gradoboeva *et al*., 2005; James *et al*., 2000) (Table 4 & Fig. 5).

Fishery Applications: Potential live vaccination has been carried out in fishery field for early protection of flounder and significant protection of Turbot from *Vibrio harveyi* by surface expression of haemolysin protein, which was engineered by *HL 1* gene of *Vibrio harveyi* SF 1 is cloned in to pYDI-1 and pYDI-2 vector and expressed in *S. cerevisiae* (Kailing Zhu *et al*., 2006). Infectious pancreatic necrosis virus (IPNV) causes pancreatic necrosis in salmonid fish with significant loss in aquatic industry. Viral Capsid protein (VP2)

Table 1. Human Gastrointestinal Applications of Recombinant probiotic *Saccharomyces cerevisiae*

Sl. No.	Host organism for expression	Desired property	Reference
1	*Saccharomyces cerevisiae*	Temperature tolerance	Daquinag *et al*., 2007
2	*Saccharomyces cerevisiae*	Acid tolerance	Hassan Hamedi *et al*., 2013; Nuno *et al*., 2010
3	*Saccharomyces cerevisiae*	pH tolerance	Arino., J. *et al*., 2010; Abdel chaek *et al*., 2007
4	*Saccharomyces boulardii*	Bile tolerance	Hassan Hamedi *et al*., 2013; Abdel chaek *et al*., 2007
5	*Saccharomyces cerevisiae*	Digestive enzymes tolerance	Trabalzini *et al*., 2003; Platara *et al*., 2006
6	*Saccharomyces boulardii*	Anaerobic condition tolerance	Lauren., H. *et al*., 2015
7	*Saccharomyces cerevisiae*	Zinc Sulphate absorption	Nuno *et al*., 2010
8	*Saccharomyces boulardii & Kluyveromyces lactis*	Vitamin B6 productivity	Ahmed *et al*., 2009
9	*Saccharomyces cerevisiae*	*Cytochrome* P450 73A1 expression	Yu *et al*., 1996; Klein *et al*., 1993; Pecquet *et al*., 1991
10	*Saccharomyces cerevisiae*	Bioconversion rate of CIN to COU	Blanquet *et al*., 2003; Garrait *et al*., 2007
11	*Saccharomyces boulardii*	5-Fluoroorotic acid, uracil and uridine tolerance	Arino., J. *et al*., 2010

Table 2. Human Therapeutic Applications of Recombinant probiotic *Saccharomyces cerevisiae*

Sl. No.	Host organism for expression	Desired property	Reference
1	*Saccharomyces boulardii*	Enhanced antimicrobial activity	Lauren., H. *et al*., 2015; Nuno *et al*., 2010; Christopher *et al*., 2010; Kuhle *et al*., 2005
2	*Saccharomyces cerevisiae*	Human serum albumin Expression	Christopher *et al*., 2010; Jens., N. *et al*., 2013; Payne *et al*., 2008
3	*Saccharomyces cerevisiae*	Insulin Expression	Stepien *et al*., 1983
4	*Saccharomyces boulardii*	Therapeutic prophylactic activity	Xinhua *et al*., 2009
5	*P. pastoris* & *Saccharomyces cerevisiae*	Urate oxidase enzyme expression	Ramin *et al*., 2014
6	*Saccharomyces cerevisiae*	Transferring (rTf) Expression	Stepien *et al*., 1983
7	*Saccharomyces cerevisiae*	Hirudin Expression	Payne *et al*., 2008; Jutta *et al*., 1994
8	*Saccharomyces cerevisiae*	GM-CSF Expression	Miyajima *et al*., 1986

Table 3. Human Immunological Applications of Recombinant probiotic *Saccharomyces cerevisiae*

Sl. No.	Host organism for expression	Desired property	Reference
1	*Saccharomyces cerevisiae*	Enhancement of host own Immune System	Lauren., H. *et al*., 2015
2	*Saccharomyces cerevisiae*	Beta lactamase expression	Rainer., R. *et al*., 1981
3	*Saccharomyces cerevisiae*	*Staphylococcus aureus nuclease A* Immunization	Pines., O. *et al*., 1981;
4	*Saccharomyces cerevisiae*	TSST-I Immunization	Robert *et al*., 1994
5	*Saccharomyces cerevisiae*	Shiga-like toxin I A-chain Immunization	Schonberger *et al*., 1991; Paul., L.P. *et al*., 2005
6	*Saccharomyces cerevisiae*	Heat labile enterotoxin Immunization	Deresiewicz *et al*., 1992; Lim *et al*., 2009
7	*Saccharomyces cerevisiae*	Cholera toxin B Immunization	Mohsen., A. *et al*., 2005; Bita Bakhshi *et al*., 2014
8	*Pichia pastoris* & *Saccharomyces cerevisiae*	Hookwarm Immunization	Gaddam., N.G. *et al*., 2004
9	*Saccharomyces Prombe* & *Saccharomyces cerevisiae*	Bloom's syndrome and Werner's syndrome Immunization	Yu *et al*., 1996; Scott., D. *et al*., 1998 Abdel *et al*., 2007
10	*Saccharomyces cerevisiae*	HBS3 (HBsAg) Immunization	Atsushi., M. *et al*., 1983; Schreuder *et al*., 1986
11	*Pichia pastoris* & *Saccharomyces cerevisiae*	Hepatitis C Immunization	Mehdi., F. *et al*., 2014
12	*Saccharomyces cerevisiae*	PEDV Immunization	Seung., M.P. *et al*., 2007
13	*Saccharomyces cerevisiae*	Cervical cancer vaccine Immunization	Walid., O. *et al*., 2005; Woo *et al*., 2008
14	*Saccharomyces cerevisiae*	Tumour Immunization	Andressa *et al*., 2010; Lim *et al*., 2009

Table 4: Veterinary Applications of Recombinant Probiotic *Saccharomyces cerevisiae*

Sl. No.	Host organism for expression	Desired property	Reference
1	*Saccharomyces cerevisiae*	Phytate degradation	Haraldsson *et al*., 2005; Yanming., H. *et al*., 1999
2	*Saccharomyces cerevisiae*	IBD Immunization	Sohini *et al*., 2009
3	*Saccharomyces cerevisiae*	Porcine pleuropneumonia Immunization	Min Kyoung Shin *et al*., 2013
4	*Saccharomyces cerevisiae*	PPV Immunization	Paulius., L.T. *et al*., 2014
5	*Saccharomyces cerevisiae*	ETEC Immunization	Roger., B. *et al*., 2012; Rezaee., M.A. *et al*., 2005
6	*Saccharomyces cerevisiae*	Bovine Interferons expression	Anastasia *et al*., 2005; James *et al*., 2000
7	*Saccharomyces cerevisiae*	pGH Expression	Chen., C.M. *et al*., 2000

Table 5. Fishery Applications of Recombinant probiotic *Saccharomyces cerevisiae*

Sl. No.	Host organism for expression	Desired property	Reference
1	*Saccharomyces cerevisiae*	*Vibrio harveyi* Immunization	Kailing Zhu et al., 2006
2	*Saccharomyces cerevisiae*	Pancreatic necrosis Immunization	Thomas., A. et al., 2007
3	*Saccharomyces cerevisiae*	Fish growth hormone expression	Huai., J. T. et al., 1994

coding gene was cloned in to pIPC1-Z1 and expressed in *S. cerevisiae,* for inducing immunization in fishes. (Thomas., A. *et al*., 2007). Fish growth hormone rainbow trout cDNA was cloned into pYERT vector and expressed in *Saccharomyces cerevisiae* under the control of glyceraldehyde-3-phosphate dehydrogenase promoter and it is orally administrated as food stuff for juvenile striped mullet (*Mugil cephalus*) for enhanced growth (Huai., J. T. *et al*., 1994) (Table 5 & Fig. 6).

FUTURE DIRECTIONS

This knowledge is helpful for the development of different Bio-Medicines in future to intercept, prevent or control the diseases and establishment of innate normal flora to protect the host immune system from foreign agents.

CONCLUSION

In modern days humans and animals are regularly exposed to bombarding with numerous chemicals, microorganisms, foods produced by using fertilizers, pesticides and microbial fermentations. Synthetic chemicals and microorganisms muddle human and animal metabolisms, the metabolic disorders lead to infections and diseases. For the control of these disorders, again synthetic drugs were being used which accumulated in the organelles of living forms, and exerted side effects there by reducing the life span. Slight modifications in the gene sequence and by expression of specific genes in beneficial organisms like probiotic *Saccharomyces cerevisiae* may results in reduction of metabolic disorders in the living forms.

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ETHICAL APPROVAL: Animals were not used for the execution of this research work.

AUTHORS AND CONTRIBUTIONS

The concept of the article, article preparation and formatting has been done by SB with the help of RM, article has been reviewed by KC and EAM. All authors read and approved the final manuscript.

REFERENCES

Abdel, C., Nivien, AA., Hassan, AL., Mohamed, A., Azzat, B. 2007. Genetic Construction of Potentially Probiotic *Saccharomyces boulardii* Yeast Strains Using Intraspecific Protoplast Fusion. J. Appl. Sci. Res., 3(3):209-217.

Ahmed, NS., Nivien, A., Rahman, A., Samir, M., Abdalla., Hassan, AL., Mohamed, A., Rasha, GSS. 2009. Impact of Some Genetic Treatments on the Probiotic Activities of *Saccharomyces boulardii.* RJCMB., 3(1):12-19.

Alric, M., Blanquet, S., Marol-Bonnin, S., Pompon, D., Renaud, M. 2000. Microorganismes actifs dans l'environnement digestif. International patent., WO:01/98461.

Anastasia, G., Mikhail, S., Marina, P. 2005. Yeast *Saccharomyces cerevisiae* and *Pichia pastoris* strains producers of intracellular bovine interferon gamma. Yeast., 22: S1-S236.

Andressa, A., Jack, P., Higgins, J., Hodge, W. 2010. Vaccines based on whole recombinant *Saccharomyces cerevisiae* cells. FEMS Yeast Res., 10:1060-1069.

Arino, J. 2010. Integrative responses to high pH stress in *S. cerevisiae*, OMICS A Jou. of Int. Bio., 14(5):517-523.

Atsushi, M., Akio, T., Chikateru, N., Fukusaburo, H., Nobuya, O., Kenichi, M. 1983. Expression of hepatitis B surface antigen gene in yeast. Proc. Natl. Acad. Sci. USA., 80:1-5.

Bhopale., Nanda, RK. 2005. Recombinant DNA expression products for human therapeutic use. Curr. Sci., 89(4):614-620.

Bita, B., Mina, B., Masoud, G. 2014. A Single Point Mutation within the Coding Sequence of Cholera Toxin B Subunit will increase its Expression Yield. IBJ., 18(3):130-135.

Blanquet, S., Marol-Bonnin, S., Beyssac, E., Pompon, D., Renaud, M., Alric, M. 2001. The biodrug concept: an innovative approach to therapy. Trends Biotechnol., 19:393-400.

Blanquet, S., Meunier, JP., Minekus, M., Marol-Bonin, S., Alric, M. 2003. Recombinant *Saccharomyces cerevisiae* expressing P450 in artificial digestive systems: a model for biodetoxication in the human digestive environment. Appl. Environ. Microbiol., 69:2884-892.

Blehaut, H., Massot, J., Elmer, GW., Levy, RH. 1989. Disposition kinetics of *Saccharomyces boulardii* in man and rat. Biopharm. Drug Dispos., 10:353-364.

Canganella, F., Paganini, S., Ovidi, M., Vettraino, AM., Bevilacqua, L., Massa, S., Trovatelli, LD. 1997. A microbiology investigation on probiotic pharmaceutical products used for human health. Microbiol. Res., 152:171-179.

Chen, CM., Chang, YC., Chen, CL., Cheng, WTK. 2000. High-Level Expression of Growth Hormone in the Methylotropic Yeast and Its Application on Growth Improvement of Fowls. Asian Aus. J. Anim. Sci., 13:157-160.

Chen, X., Fruehauf, J., Jeffrey, D., Goldsmith., Hua Xu., Kianoosh, K., Katchar., Koon, H., Zhao, D., Efi, G., Kokkotou., Pothoulakis, C., Ciaran., Kelly, P. 2009. *Saccharomyces boulardii* inhibits EGF receptor signaling and intestinal Tumor growth in Apcmin mice. Gastroenterology, 137:914-923.

Christopher, JA., Finnis., Tom, P., Joanna, H., Neil, D., Diane, W., Philip, M., Malcolm, JS., David, JT., Robert, WE., Hans, G., Barbara, SM., Nina, T., Darrell, S. 2010. High-level production of animal free recombinant transferrin from *Saccharomyces cerevisiae*. MCF., 9(87): 1475-2859.

Corthier, G., Renault, P. 1999. Future directions for research on biotherapeutic agents: contribution of genetic approaches on lactic acid bacteria. 269–304. In Elmer, G. W., McFarland, L., Surawicz, C., (ed.), Biotherapeutic agents and infectious diseases. Humana Press, Inc., Totowa, NJ.

Dae, KC., Dong, HS., Byung, WK., Jae, KN., In Seob, H., Soo, WN. 1997. Expression and secretion of *Clostridium thermocellum* endoglucanase A gene (celA) in different *Saccharomyces cerevisiae* strains. Biotechnology Letters., 19(6):503-506.

Daquinag, A., Fadri, M., Jung, SY., Qin, J., Kunz, J. 2007. The yeast PH domain proteins Slm1 and Slm2 are targets of sphingolipid signaling during the response to heat stress, Mol. Cell. Biol., 27(2):633-650.

Deresiewicz, RL., Calderwood, SB., Robertus, JD., Collier, RJ. 1992. Mutations effecting the activity of the shiga-like toxin I A-chain. Biochem., 31:3272-3280.

Dey, S., Upadhyay, C., Mohan, CM., Kataria, JM., Vikram, N., Vakharia. 2009. Formation of subviral particles of the capsid protein VP2 of infectious bursal disease virus and its application in serological diagnosis. J. Virol. Methods., 157:84-89.

Drouault, S., Juste, C., Marteau, P., Renault, P., Corthier, G. 2002. Oral Treatment with *Lactococcus lactis* Expressing Staphylococcus hyicus Lipase Enhances Lipid Digestion in Pigs with Induced Pancreatic Insufficiency. Appl. Environ. Microbiol., 68 (6):3166-3168.

Elizabeth, K., Wansley, MC., Kenneth, W., Hance., Michae, B., Bernstein., Amanda, L., Boehm., Zhimin, G., Deborah, Q., Alex., John. W., Greiner., Schlom, J., James, W., Hodge. 2008. Vaccination with a recombinant *Saccharomyces cerevisiae* expressing a tumor antigen breaks immune tolerance and elicits therapeutic antitumor responses. Clin. Cancer Res, 14(13):4316-4325.

Ellis, NA., Groden, J., Ye, TZ., Straughen, J., Lennon, DJ., Ciocci, S., Proytcheva, M., German, J. 1995. The Bloom's syndrome gene product is homologous to RecQ helicases. Cell, 83:655-666.

Fahl, WE., Loo, D., Manoharan, H. 1999. Chemoprotective bacterial strains. International patent, WO:99/27953.

Fazel, R., Zarei, N., Ghaemi, N., Namvaran, MM., Enayati, S., Ardakani, EM., Azizi, M., Khalaj, V. 2014.Cloning and expression of Aspergillus flavus urate oxidase in Pichia pastoris. Springer Plus, 3(395):1-7.

Gaddam, NG., Bin, Z., Kashinath, G., Loukas, A., Hawdon, J., Dobardzic, A., Deumic, V., Liu, S., Dobardzic, R., Bernard, C., Zook., Jin, Q., Liu, Y., Hoffman, L., Debose, SC., Patel, R., Mendez, S., Peter, J., Hotez. 2004. Cloning, Yeast Expression, Isolation, and Vaccine Testing of Recombinant Ancylostoma-Secreted Protein (ASP)–1 and ASP-2 from Ancylostoma ceylanicum. J. Infect. Dis., 189:919-929.

Garrait, G., Jarrige, JF., Blanquet, S., Beyssac, E., Alric, M. 2007. Recombinant *Saccharomyces cerevisiae* Strain Expressing a Model Cytochrome P450 in the Rat Digestive Environment: Viability and Bioconversion Activity. Applied and Environmental Microbiology. ,73(11):3566-3574.

Hamedi, H., Misaghi, A., Modarressi, MH., Salehi, TZ., Khorasanizadeh, D., Khalaj, V. 2013. Generation of a Uracil Auxotroph Strain of the Probiotic Yeast *Saccharomyces boulardii* as a Host for the Recombinant Protein Production. Avicenna J. Med. Biotech., 5(1):29-34.

Haraldsson, AK., Veide, J., Andlid, T., Alminger, ML., Sandberg, AS. 2005. Degradation of phytate by high phytase *Saccharomyces cerevisiae* strains during simulated gastrointestinal digestion. J. Agric. Food Chem., 53:5438-5444.

Huai, JT., Kuo, JC., Lou, SW., Kuo, TT. 1994. Growth Enhancement of Juvenile Striped Mullet by Feeding Recombinant Yeasts Containing Fish Growth Hormone. Prog. Fish-Cult., 56 (1):7-12.

James, K., Pru., Kathy, J., Austin., David, J., Perry., Alisha, M., Nighswonger., Thomas, R., Hansen. 2000. Production, Purification, and Carboxy Terminal Sequencing of Bioactive Recombinant Bovine Interferon Stimulated Gene Product. Biol. Reprod., 63:619-628.

Jens, N. 2013. Production of biopharmaceutical proteins by yeast, Advances through metabolic engineering. Bioengineered, 4(4):207-211.

Jutta, H., Takabayashi, K., Meyhack, B., Marki, W., Pohlig, G.1994. C-terminal proteolytic degradation of recombinant desulfato hirudin and its mutants in the yeast *Saccharomyces cerevisiae*. Eur. J. Biochem., 226:341-353.

Klein, SM., Elmer, GW., McFarland, LV., Surawicz, CM., Levy, RH. 1993. Recovery and elimination of the biotherapeutic agent, *Saccharomyces boulardii*, in healthy human volunteers. Pharm. Res., 10:1615-1619.

Kopp-Hoolihan, L. 2001. Prophylactic and Therapeutic uses of probiotics: a review. J. Am. Diet. Assoc., 101:229-238.

Kuhle, A., Skovgaardij, A., Jaspersen, L. 2005. In vitro screening of probiotic properties of *Saccharomyces cerevisiae var. boulardii* and food borne Saccharomyces cerevisiae straits. Int. J. Food Microbiol., 101:29-39.

Lauren, H., McDermott, C., Fasken, M., Kuiper, E., Guiliano, D., McBride, S., Corbett, A., Lamb, T. 2015. Evaluating use of the probiotic yeast *Saccharomyces boulardii* for the synthesis and delivery of oral therapeutics (VAC8P.1061). J. Immunol., 194(1):144.17.

Lim., Jung, Gu., Kim, JA., Chung, HJ., Kim, JTG., Kim, UM., Lee, KR., Park, SM., Yang, MS., Kim, DH. 2009. Expression of Functional Pentameric Heat Labile Enterotoxin B Subunit of Escherichia coli in *Saccharomyces cerevisiae*. J. Microbiol. Biotechnol., 19(5):502-510.

Mehdi, F., Keyvani, H., Monavari, SHR., Mollaie, HR. 2014. Recombinant Core E1E2 Protein Expressed in *Pichia pastoris* Yeast a Candidate Vaccine for Hepatitis C Virus. JAA., 6(3): 139-147.

Miyajima, A., Otsu, K., Schreurs, J., Bond, MW., Abrams, JS., Arai, K. 1986. Expression of murine and human granulocyte - macrophage colony stimulating factors in *S. cerevisiae*: mutagenesis of the potential glycosylation sites. EMBO J., 5(6):193-197.

Mohsen, A., Rezaee, A., Shahrokhi, N., Hussini, AZ., Yasuda, Y., Tochikubo, K., Rezaee, MA. 2005. Expression of cholera toxin B subunit in *Saccharomyces cervisiae*. Ann. Microbiol., 55(2):145-150.

Nuno, P., Mira., Palma, M., Joana, F., Guerreiro., Correia, IS., 2010. Genome wide identification of *Saccharomyces cerevisiae* genes required for tolerance to acetic acid. MCF., 9(79):1-13.

Paul., LP., Wei, JX., Gariepy, E. 2005. A Role for the Protease-sensitive Loop Region of Shiga-like Toxin 1 in the Retrotranslocation of its A1 Domain from the Endoplasmic Reticulum Lumen. J. Biol. Chem., 280(24):23310-23318.

Paulius., LT., Burneikien, RP., Lasickien, R., Akatov, A., Kundrotas, G., Sereika, V., Lelesius, R., Cvirblien, A., Sasnauskas, K. 2014. Generation of Recombinant Porcine Parvovirus Virus like Particles in *Saccharomyces cerevisiae* and Development of Virus-Specific Monoclonal Antibodies. J. Immunol. Res., 24:1- 9.

Payne, T., Finnis, LC., Evans, DR., Mead, J., Avery, SV., Archer, DB., Sleep, D. 2008. Modulation of Chaperone Gene Expression in Mutagenized *Saccharomyces cerevisiae* Strains Developed for Recombinant Human Albumin Production Results in Increased. Production of Multiple Heterologous Proteins. Appl. Environ. Microbiol., 74 (24):7759-7766.

Pecquet, S., Guillaumin, D., Tancrede, C., Andremont, A. 1991. Kinetics of *Saccharomyces cerevisiae* elimination from the intestines of human volunteers and effect of this yeast on resistance to microbial colonization in gnotobiotic mice. Appl. Environ. Microbiol., 57:3049-3051.

Pines, O., London, A. 1991. Expression and Secretion of S*taphylococcus nuclease* A in yeast; effect of amino terminal sequences. J. Gen. Microbiol., 137:771-778.

Platara, M., Ruiz, A., Serrano, R., Palomino, A., Moreno, F., Arino, J. 2006. The transcriptional response of the yeast Na+ ATPase ENA1 gene to alkaline stress involves three main signalling pathways. J. Biol. Chem., 281(48):36632-36642.

Prakash, S., Chang, TMS. 2000. In vitro and in vivo uric acid lowering by artificial cells containing microencapsulated genetically engineered E. coli DH5 cells. Int. J. Artif. Organs, 23(7): 429-35.

Primrose, SB. 1986. The application of genetically engineered microorganisms in the production of drugs. J. Appl. Bacteriol., 61:99-116.

Querol, A., Belloch, C., Fernandez-Espinar MT., Barrio, E. 2003. Molecular evolution in yeast of biotechnological interest. Int. J. Microbiol., 6:201-205.

Rainer, R., Kuhn, BK., Cornelis, P., Hollenberg. 1981. Expression and processing of bacterial β-lactamase in the yeast *Saccharomyces cerevisiae*. Proc. Natl. Acad. Sci. USA, 78(7): 4466-4470.

Rezaee, MA., Rezaee, A., Moazzeni, SM., Salmanian, AH., Yasuda, Y., Tochikubo, K., Pirayeh, SN., Arzanlou, M. 2005. Expression of *Escherichia coli* heat labile enterotoxin B subunit (LTB) in *Saccharomyces cerevisiae*. J. Microbiol., 43(4):354-360.

Robert, L., Deresiewicz, Jesse, A., Flaxenburg, Chan, M., Robert, W., Finberg., Kasper, DL. 1994. Intracellular Expression of Toxic Shock Syndrome Toxin 1 in *Saccharomyces cerevisiae*. Infect. Immun., 26(6):2202-2207.

Roger., B., Zanello, G., Chevaleyre, C., Lizardo, R., Meurens, F., Martinez, P., Brufau, J., Salmon, H. 2012. Effect of *Saccharomyces cerevisiae var. Boulardii* and β-galactomannan oligosaccharide on porcine intestinal epithelial and dendritic cells challenged in vitro with *Escherichia coli* F4 (K88). Vet. Res., 43(4):1-11.

Schonberger, O., Hirst TR., Pines, O. 1991. Targeting and assembly of an oligomeric bacterial enterotoxiod in the endoplasmic reticulum of *Saccharomyces cerevisiae*. J. Mol. Biol., 5: 2663-2671.

Schreuder, MP., Deent, C., Boersma, WJA., Pouwels, PH., Klis, FM. 1996. Yeast expressing hepatitis B virus surface antigen determinants on its surface: implications for a possible oral vaccine. Vaccine, 14(5):383-388.

Scott, D., Christine., Han, S., Sarah, A., Ramer., Jennifer, C., Klassen., Jacobson, A., Eisenberger, A., Kevin, M., Hopkins.,

Howard, B., Lieberman., Greg, A., Freyer. 1998. Fission Yeast rad12 Regulates Cell Cycle Checkpoint control and is Homologous to the Bloom's Syndrome Disease Gene. Mol Cell Biol., 18(5):2721-2728.

Seung, MP., Mo, AY., Lim, JG., Chung, HJ., Kim, TG., Kim, KJ., Cho, DH., Moon Sik Yang, MS., Kim, DH. 2007. Surface Displayed Expression of a Neutralizing Epitope of Spike Protein from a Korean train of Porcine Epidemic Diarrhea Virus. BBE., 12:690-695.

Shin, MK., Kang, ML., Jung, MH., Cha, SB., Lee, WJ., Kim, JM., Kim, DH., Yoo, HS. 2013. Induction of protective immune responses against challenge of *Actinobacillus pleuropneumoniae* by oral administration with *Saccharomyces cerevisiae* expressing Apx toxins in pigs. Vet. Immunol. Immunopathol., 151:132-139.

Srinivas, B., Rani, GS., Kumar, BK., Chandrasekhar, B., Krishna, KV., Devi, TA., Bhima, B. 2016. Evaluating the probiotic and therapeutic potentials of *Saccharomyces cerevisiae* strain (OBS2) isolated from fermented nectar of toddy palm. AMB Express. 7(2): 1-14.

Srinivas, B., Tangutur, AD., Anthappagudem, A., Ramaiah, J., Bhukya, B. 2020. Cloning and in vivo metabolizing activity study of CYP3A4 on amiodarone drug residues: A possible probiotic and therapeutic option. Biomedicine & Pharmacotherapy, 127(2020):110128.

Stepien, PP., Brousseau, R., Wu, R., Narang, S., Thomas, DY. 1983. Synthesis of a human insulin gene VI, expression of the synthetic proinsulin gene in yeast. Gene, 24(2-3):289-97.

Thomas., A., F. C., Robert, M., Bowers., Christopher, G., Rowe., Vikram, N., Vakharia., Scott, E., La Patra., Arun, K., Dhar. 2007. Antigenicity of infectious pancreatic necrosis virus VP2 subviral particles expressed in yeast. Vaccine, 25:4880-4888.

Trabalzini, L., Paffetti, A., Scaloni A. 2003. Proteomic response to physiological fermentation stresses in a wild type wine strain of *Saccharomyces cerevisiae*. Biochem. J., 370 (1):35-46.

Umezu, K., Amaya, T., Yoshimoto, A., Tomita, K. 1971. Purification and properties of orotidine-5'-phosphate pyrophosphorylase and orotidine-5'-phosphate decarboxylase from baker's yeast. J. Biochem., 70 (2):249-262.

Walid, O., Terentjev, Y., Oliver, S. 2005. Lubomira Stateva. Towards cancer vaccine made from recombinant yeast cells. Yeast, 22:S1-S236.

Woo, MK., An JM., Kim JD., Park, SN., Kim HJ. 2008. Expression and purification of human Papillomavirus 18 L1 virus-like particle from *Saccharomyces cerevisiae*. Arch. Pharm. Res, 31(2):205-209.

Yanming., H., David, B., Wilson., Xin Gen Lei. 1999. Expression of an Aspergillus niger Phytase Gene (phyA) in *Saccharomyces cerevisiae*. Appl. Environ. Microbiol., 65(5):1915-1918.

Yu, CE., Oshima, J., Fu, YH., Wijsman, EM., Hisama, F., Alisch, R., Matthews, S., Nakura, J., Miki, T., Ouais, S., Martin, GM., Mulligan, J., Schellenberg, GD. 1996. Positional cloning of the Werner's syndrome gene. Science, 272:258-262.

Zhu, K., Chi, Z., Li, J., Zhang, F., Li, M., Yasoda, HN., Longfei, Wu. 2006. The surface display of haemolysin from Vibrio harveyi on yeast cells and their potential applications as live vaccine in marine fish. Vaccine, 24:6046-6052.

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