

Appendix 6a-English. Details of a medical contribution from Jd's Medical Family, page 2: Research Reports on PAPP-A. By PubMed & Websites (eg, Google). p71, Rd'18 (JEr. 7-1-'18
PubMed lists titles & abstracts of medicine related periodicals in the US National Library of Medicine (**2604 titles on PAPP-A by May 3, 2018**): A*, no. of titles listed by "PAPP-A Search"; B**, word "PAPP-A" in title, abstract /or text. It may exclude title without word "PAPP-A" or "pregnancy associated plasma protein A (abstract or text may have them)"; research reports at academic meets #; article in a book / monograph ## and thesis ###. **Google** Search (a, b, c,...) also lists no. citations (C*, search by "Tsue Ming Lin" 3-2-'18; D*, by article title 5-5-'18).
Abbreviations / other: E*, ID no. in my Tsue Ming Lin's CV; PAPPs = pregnancy-associated plasma proteins; pregnancy proteins, PPs; PZP, pregnancy zone protein; &, and..

Year	No. titles	Report (author: title, journal/ 'book' name & volume: pages.)	No citations	Note
A*	B**	Mine Others'	C* D* E*	2
		Note 1: <--Significance of this report.	Notes 3-7	
1958	0	0	### Thornes RD: Proteins of pregnancy, MD thesis, U Dublin, 64 p; <--World 1st research record of pregnancy proteins.	Note 7
1971	0	0	Bohn H: Detection & characterization of pregnancy proteins in the human placenta & their quantitative...in sera from pregnant women, Arch Gynaekol 210: 440-57. <--Several PAPPs, but no PAPP-A.	Note 7
1972	0	0	Gall SA & Halbert SP: Antigenic constituents in pregnancy plasma which are undetectable in normal non-pregnant female or male plasma, Int Arch Allergy 42: 503-15. <--Revealed several PPs as above 2 papers, but no PAPP-A either.	Note 7
1973	0	#	Lin, et al.: Characterization & purification of PAPP's, Fed Proc 32 (3): 623. <-- World 1st report on PAPP-A	Notes 5 & 8
1974	2	1	*** Lin et al.: Characterization of four PAPP's, Am J Obstet Gynecol 118: 223-236. <--Often cited as 1st report on PAPP-A	Note 2
			*** Lin et al.: PAPP's in the rat & mouse, Proc Soc Exp Biol Med 145: 62-66.	Note 5
			# Lin et al.: Measurement of PAPP's during gestation & their immunological identification, Fed Proc 33: 282.	Note 5
			*** Lin et al.: Three PAPP's: Purification, monospecific antisera & immunological identification, Int Arch Allergy 47: 35-53.	Note 5
			Lin et al.: Measurement of PAPP's during human gestation, J Clin Investig 54: 576-82. <--PubMed's 1st list on PAPP-A	Note 7
1975	2	1	Lin et al.: Immunological comparison of various human PAPP's, Int Arch Allergy 48: 101-115. # Lin et al.: PAPP's in human placenta, Fed Proc 34: 682.	
1976	7	4	Lin et al.: Human PAPP's during the postpartum period, Am J Obstet Gynecol 124:382-387. Lin et al.: Relation of obstetric parameters to the concentrations of four PAPP's at term in normal gestation, Am J Ob Gyn 125: 17-24. <--First noted high PAPP-A in pregnancy with high blood pressure(the first of 2 major signs for pre-eclampsia).	Note 3
			Lin et al.: Quantitative analysis of PAPP's in human placenta, J Clin Investig 57:466-47. *** Lin et al.: PZP analogue in pregnant & non-pregnant primates, & its decrease during pregnancy in some momkey species, Clin Exp Imm 26: 609-622. Lin & Halbert: Placental localization of human PAPP's, Science 193:1249-1252. <--Published soon, 3 months after submission.	165 j
1977	2	1	Lin et al.: Plasma concentration of 4 PP in complications of pregnancy, Am J Obs Gyn 128: 808-810. <--2nd on high PAPP-A in toxemia	38 k
			### Kiefer: An investigation into the immunosuppressive properties of pregnancy serum, U Miami PhD thesis, 159 pages. = pre-eclampsia	
1978	4	1	Lin et al.: Immunological relationship of human & subhuman primate PAPP's, Int Arch Allergy 56: 207-223. *** Lin et al.: Characterization & purification of PAPP-B, Int Arch Allergy 57: 294-303. *** Lin et al.: PAPP's in pregnant & pseudopregnant rats, Int Arch Allergy 57: 233-238. *** Lin et al.: PAPP-B in normal & abnormal pregnancies at term, Brit J Obstet Gynecol 85: 652-656. # Home et al (6 corresp. authors): human placental & pregnancy proteins, Scan J Immunol 8 (S8): 55-64. (A report, intern. meet)	Note 4
1979	7	3	Bischof P: Purification & characterization of PAPP-A, Arch Gynecol 227:315-26. <--1st PubMed list on PAPP-A by other labs. ## Halbert & Lin: PAPP-A & PAPP-B, 'Placental Proteins' p89-103, (ed Klopfer & Chard), Springer-Verlag, '79. (Invited oral review in Scotland '78).	Note 2
1980	12	5	Hughes et al.: Assay of PP to determine fetal risk, Br Med J 280: 671-3. <--1st on PAPP-A in pre-eclampsia by other labs.	
1981	16	11	(After my test, Daco Corp. made & sold animal antibody for assaying PAPP-A).	Note 4
1982	19	15	Sutcliffe et al.: Studies on ...PAPP-A during ... & complicated pregnancy, Placenta 3: 71-80. <--1st on low PAPP-A in pregnancy with diabetes. ## Lin & Halbert: Identification, purification & characterization of PAPP-A & PAPP-B, 'Pregnancy Proteins - Biology, Chemistry & Clinical Application' p 283-312 (ed., Grudzinskas et al), Acad Press. (Invited review for Int Conf. Austria, see Appdx 6, p56). ## Bischof et al: A hypothesis on the biological function of PAPP-A, p321-332 in the above book.	Note 7
1983	32	27	# Lin: Immunological application & implication of pregnancy proteins, Chinese J Microb Imml 16: 116-117. (Invited oral review in Intern. Conf. Taipei '83).	
1984	38	31	*** Lin TM: Immunological application & implication of pregnancy proteins", Chinese J Microb Immunol 17: 25-35. (Invited review). ## Bischof : PAPP-A, 'Placetal Proteins' p 41-73, Karger.	Note 2
1985	28	20	Note 2: This 1974 paper \$ is often cited as 'discovered', "first identified", 'originally isolated' or "originally identified" PAPP-A by papers like \$ and \$\$. PAPP-A is listed in PubMed with its full title only. > 80 % of >2,500 articles listed in PubMed do not mention the 1st report on PAPP-A . The Bischof 1984 monograph \$\$\$ mistakes the Gall & Halbert 1972 paper \$\$\$ to have reported the discovery of PAPP-A. Home et al 1979 report \$\$\$ had me & my boss Halbert as corresponding member / author in its draft but, as I found 40 years later, not in the published. We both were invited to the meeting but did not go as it offered insufficient travel expenses (meeting in Denmark. See Appendix 6, p56 for detail).	
1986	26	22		
1987	16	9		
1988	15	9		
1989	20	15		
1990	13	9	## Brambati et al.: Ultrasound & biochemical Assessment of 1st trimester prgnancy,'The Embryo:...' p181-194. <--1st on low PAPP-A in pregnancy with Down Syndrome fetus (PDSF).	
1991	9	5		
1992	6	3	Wald et al.: First trimester concentration of PAPP-Ain Down syndrome, BMJ 305: 28. <--2nd paper on low PAPP-A in PDSF.	146 s
1993	29	17	Note 3: By June 30, 2018, PubMed lists 2626 titles on PAPP-A, mostly in relation to diseases (e.g., Down syndrome fetus, > 620 titles; early detection of pre-eclampsia, 277; cardiovascular diseases, 293 & review, 288).	
1994	24	15	Note 4: Google lists more than 30 vendors selling animal antibodies to & assay kits for PAPP-A of human (gene on chromosome 9), apes (9), monkey (15), horse, cattle (8), Kangaroo, pig, dog (11), cat, rat (5), mouse (4), chicken (17), frog, zebrafish (5) & shark (1). It's protease activity is used for assaying lower animal's PAPP-A. Our 3rd 3-year NIH research grant application was to assay PAPPs in 7,000 serum samples on hand for its relation with abnormal pregnancies & to use 600 monkeys for contraceptive / pregnancy termination effect. Animal protection activities (e.g., Human Society) were very high then, made our plan too low score to be funded.	
1995	24	16	Lawrence et al.: The insulin-like growth...protease is PAPP-A, Proc Natl Acad Sci 96: 3149-53. <--2 labs showed a protease	Note 6, 2
1996	24	13	Conover et al.: Evidence that the insulin-like...is PAPP-A, J Clin Endocrin Med 84: 4742-5. for IGFBP-4 as PAPP-A.	723 t
1997	23	14	Most titles in A* are in B** since year 2000, but might not include those using PAPP-A's other terms such as IGFBP-4 protease, pappalysin, D1PLA1, ASBABPZ, etc.	125 u
1998	18	9	Bayes-Genis et al.: PAPP-A as a marker of acute coronary syndromes, N Egl J Med 345: 1022-9. <--1st 2 reports	Note 2
1999	39	29	Futterman et al.: Novel markers in the ACS: BNP, IL-6, PAPP-A.", Am J Crit Care 11: 168-72. on high PAPP-A in acute heart d.	854 v
2000	36	27	Note 5: PubMed Search neither list article on PAPP-A in book, monograph, thesis, & meeting records, nor animal PAPP-A in some biological journals. For PAPP-A, it could contain titles related to PAPP-A or unrelated by authors with PAPP as name.	85 w
2001	54		Note 6: This protease had many names such as " insulin-like growth factor (IGF)-dependent IGF binding protein-4 protease & now PAPP-A. Like insulin, it indirectly increases cell growth (by IGF1 for late & IGF2, early phases) & related to trisomy formation of chromosome 21 of Down syndrome fetus, but no detail yet.	
2002	70		Note 7: Two scores of labs reported pregnancy proteins using similar lab procedures since 1958, including my boss' (Dr. Halbert) labs at Colombia U previously &, before I joined, at U Miami. By our initiation in early 1970s, reagents were exchanged and their reactivities compared, > 12 with different names such as pregnancy zone protein (PZP) were shown to be the same protein and, as also confirmed at later international meets, PAPP-A and PAPP-B are new discoveries. Some investigators there and in writing asked why we in Mimai are the first to reveal these 2 proteins in 1973	
2003	74		Note 8: An oral report of discovery, isolation, purification, characterization & designation as PAPP-A, -B, -C & -D from plasma of pregnant women at the annual joint convention of basic medical societies (physiology, biochemistry, pharmacology, pathology, immunology, nutrition, etc) with near 30,000 attendants. Its abstract was submitted by Dec. 14, 1972 for review & appeared in "Federation Proceeding" March volume for members to read. Therefor, PAPP-A came to being in December 1972.	
2004	89		Cai, et al.: Association of PAPP-A level with essential hypertension....in Chinese population: ...20 research studies ... 3332	Note 2
2005	122		individuals, BML Open 2015 Sept 28:5(9):e008210.	2 x
2006	118			
2007	116			
2008	130			
2009	131			
2010	169			
2011	177			
2012	166			
2013	192			
2014	188			
2015	174			
2016	149			
2017	165	Two new fields:	Rauouli, et al.(> 300 authors): Rare and low frequency coding variants alter human adult height, Nature 542:186-190. Its abstract: "...rare height-increasing alleles of STC2 compromised ...of PAPP-A and ... resulting in higher bioavailability of insulin-like growth factors." Mihelcic et al.: Using redescription mining to relate clinical & biological characteristic of cognitively impaired and Alzheimer disease patients, PLoS One 12: e0187364. It concludes "... discovery of one largely unknown attribute: the PAPP-A....highly associated with cognitive impairment in Alzheimer disease..."	