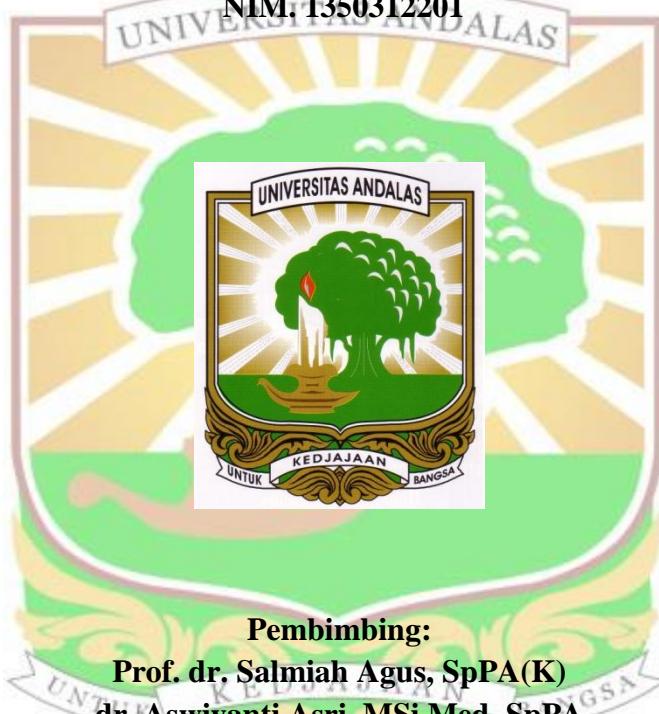


**Analisis Ekspresi TOPO2A dan HER-2 serta Hubungannya  
dengan Faktor Prognostik Histopatologik Karsinoma  
Payudara Invasif Tidak Spesifik**

TESIS

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**PROGRAM PENDIDIKAN DOKTER SPESIALIS-1 PATOLOGI  
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# **ANALISIS EKSPRESI TOPO2A DAN HER-2 SERTA HUBUNGANNYA DENGAN FAKTOR PROGNOSTIK HISTOPATOLOGIK KARSINOMA PAYUDARA INVASIF TIDAK SPESIFIK**

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## **Abstrak**

**Pendahuluan:** Resistensi pengobatan yang ditandai dengan kekambuhan lokal-regional serta timbulnya efek samping sistemik yang hebat terhadap terapi non-bedah salah satu penyebab tingginya angka kematian pada penderita karsinoma payudara saat ini. Kemoterapi berbasis *anthracycline* diketahui lebih efektif mencegah kekambuhan lokal-regional namun berisiko terhadap kegagalan jantung sehingga dibutuhkan penanda spesifik untuk pemberian kemoterapi ini. TOPO2A merupakan molekul target direk *anthracycline*. Ekspresi protein dan kelainan gen TOPO2A diduga dapat dijadikan indikator pemberian *anthracycline* akan tetapi hasil penelitian saat ini masih ditemukan kontroversi. Kelainan gen TOPO2A selalu dikaitkan dengan amplifikasi gen HER-2 karena keduanya terletak pada kromosom yang sama dan diduga berhubungan dengan sensitifitas terhadap kemoterapi berbasis *anthracycline*.

**Metode:** Penelitian ini merupakan penelitian observasional dengan desain *cross sectional*. Sampel penelitian sebanyak 50 kasus karsinoma payudara invasif tidak spesifik yang didiagnosis di Sentra Diagnostik Patologi Anatomik Fakultas Kedokteran Universitas Andalas periode tahun 2014-2015 yang dilakukan re-evaluasi terhadap jumlah mitosis dan derajat histopatologik serta kemudian dilakukan pulasan imunohistokimia dengan antibodi TOPO2A dan HER-2. Ekspresi TOPO2A dan HER-2 dinilai masing-masing pada inti dan membran sel. Hubungannya dengan jumlah mitosis dan derajat histopatologik dianalisis dengan menggunakan uji statistik *T-test*, *Oneway Anova* dan *Chi square test* dengan nilai  $p<0,05$  dianggap sebagai bermakna.

**Hasil:** Ekspresi TOPO2A dan HER-2 positif masing-masing ditemukan pada 18 kasus (36%) dan 10 kasus (20%). Analisis statistik menunjukkan hubungan yang bermakna antara overekspresi TOPO2A dengan jumlah mitosis ( $p=0.004$ ) dan derajat histopatologik ( $p=0.006$ ), serta tidak terdapat hubungan yang bermakna antara overekspresi HER-2 dengan jumlah mitosis ( $p=0.72$ ) dan derajat histopatologik ( $p=1,000$ ).

**Diskusi:** Overekspresi protein TOPO2A secara konsisten berhubungan dengan karsinoma payudara yang agresif dibandingkan dengan overekspresi HER-2 dan dapat digunakan sebagai penanda prognostik terhadap pemberian kemoterapi berbasis *anthracycline*.

**Kata kunci:** Karsinoma payudara invasif tidak spesifik, TOPO2A, HER-2

# **ANALYSIS EXPRESSIONS OF TOPO2A AND HER-2 AND THEIR CORRELATIONS WITH HISTOPATHOLOGICAL PROGNOSTIC FACTORS OF INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE**

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## ***Abstract***

**Introduction:** Resistance to treatment which is characterized by local-regional recurrence and severe systemic side effects due to non-surgery therapy are thought to be one cause of high breast carcinoma mortality rate recently. Anthracycline based chemotherapy has been known more effectively to reduce local-regional recurrence but have a risk of cardiac failure so a specific marker was needed for this chemotherapy. TOPO2A has known as a direct molecular target of anthracycline. TOPO2A protein expressions and gene alterations were assumed as indicator of anthracycline administration but still there were controversies in result. TOPO2A gene alterations were associated with HER-2 gene amplification because they both were located adjacent in the same arm of chromosome and were assumed to have correlation with sensitivity to anthracycline based chemotherapy.

**Methods:** This research was a retrospective observational cross-sectional study with a total of fifty cases invasive breast carcinoma of no special type that were diagnosed in The Anatomical Pathology Center of Diagnostic, Medicine Faculty of Andalas University at year 2014-2015. Samples were reviewed for mitotic count and histopathological grade and then stained with TOPO2A and HER-2 antibodies immunohistochemically. TOPO2A and HER-2 expressions were evaluated in nuclear dan membrane cells respectively. Their correlations with mitotic count and histopathological grade were analyzed by T-test, One way Anova and Chi square test with  $p<0,05$  was considered significance.

**Results:** TOPO2A and HER-2 expression were found positive in 18 (36%) and 10 cases (20%), respectively. There were significant correlations between TOPO2A overexpression with mitotic count ( $p=0.004$ ) and histopathological grade ( $p=0.006$ ), but there were no significant correlations between HER-2 overexpression with mitotic count ( $p=0.72$ ) and histopathological grade ( $p=1,000$ ).

**Discussion:** Overexpression of TOPO2A protein was consistently correlate with aggressive breast carcinoma compared than HER-2 and can be use as a prognostic indicator of anthracycline based chemotherapy administration.

**Keywords:** Invasive breast carcinoma of no special type, TOPO2A, HER-2