

ESSURE

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PHYSIOPATHOLOGIE : TOXICITÉ CUTANÉE

NICKEL :

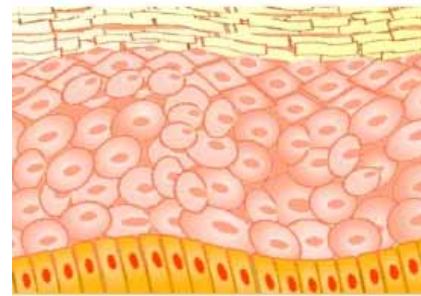
allergène de contact le plus fréquent en Europe et pays industrialisés

(Ahlström et al. Contact Dermatitis, 2019)

- **Allergie au métal**
- **Allergie aux sels de nickel soluble**
- **Allergie concomitante aux métaux : nickel, chrome, cobalt, palladium**
 - **Dermatite allergique de contact**
 - **Urticaire de contact**
 - **Dermatite de contact systémique**

CONSÉQUENCE DE L'EXPOSITION DE LA PEAU AUX ALLERGÈNES DE CONTACT

Molécules allergisantes
=
haptènes



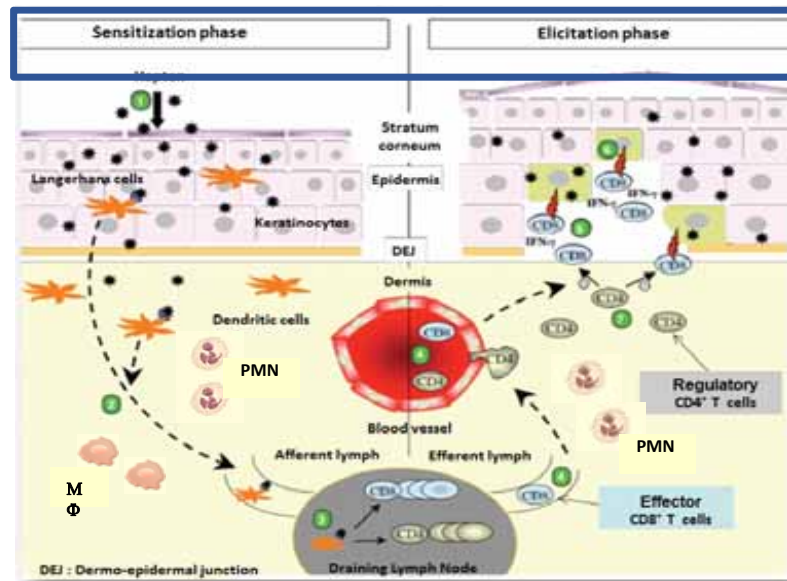
Henna tattoo



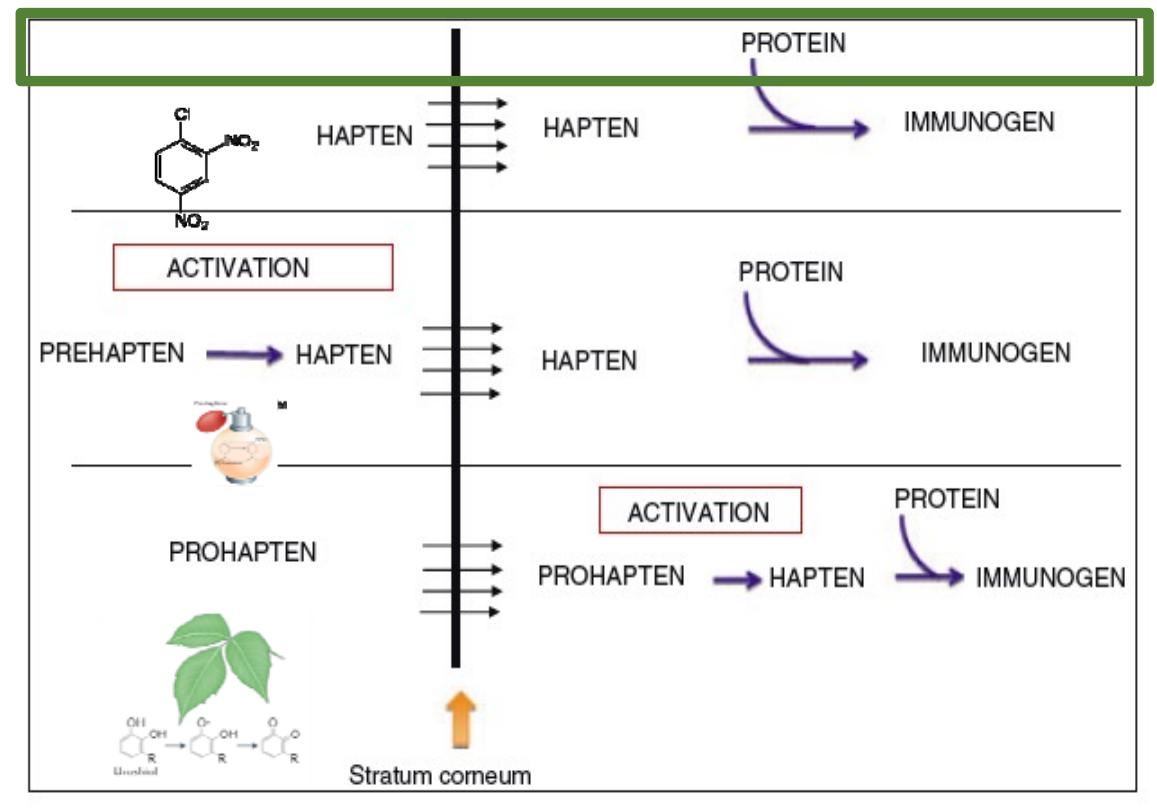
Evans et al., New Eng. J. Med. 2008

**Allergie cutanée
Dermatite allergique de contact (DAC)**

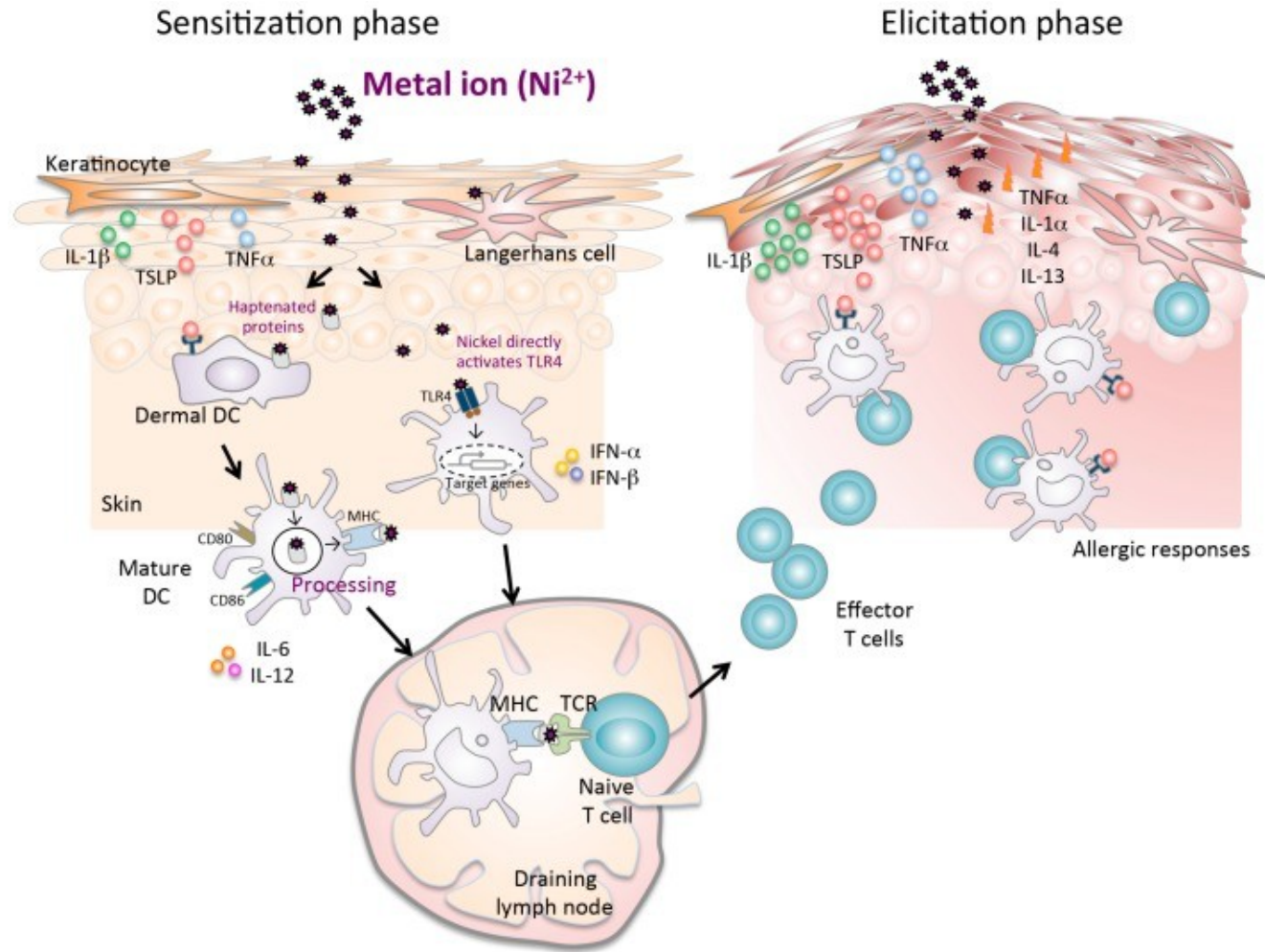
DAC ET HAPTÈNES



La réactivité chimique joue un rôle important.



NICKEL ET DAC



Saito et al., International J. of Molecular Sciences, 2016

NICKEL ET DAC

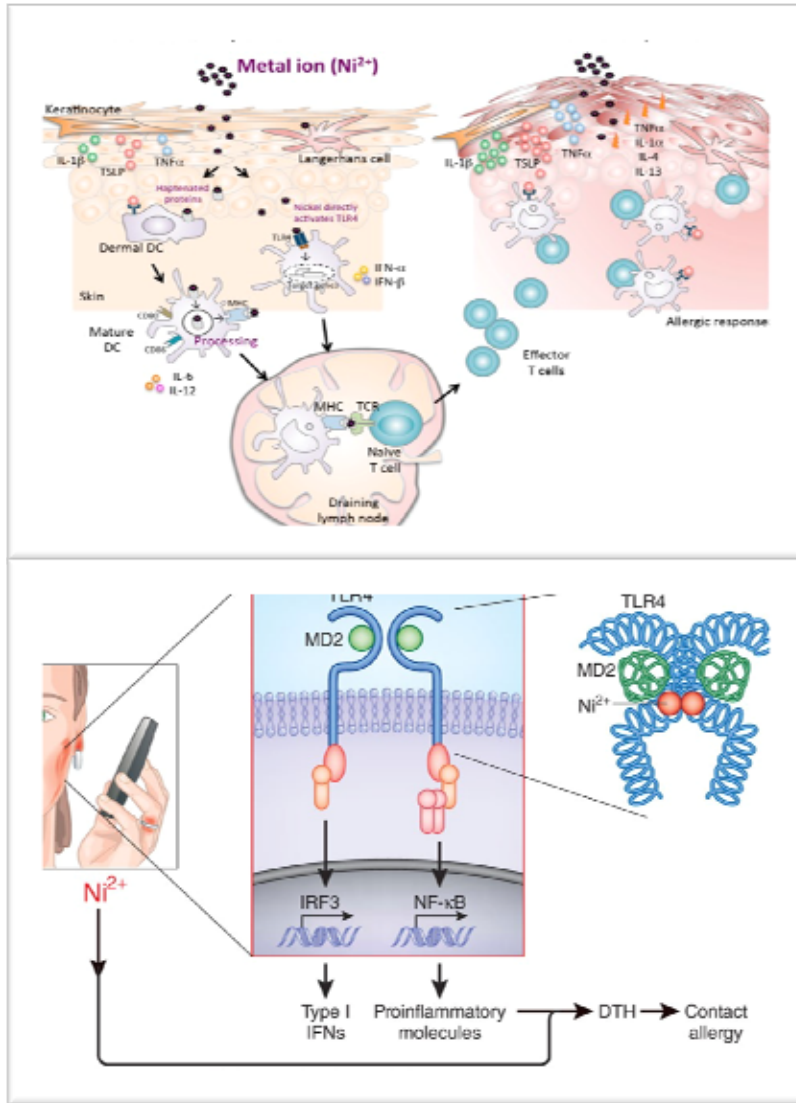
- Dermatite allergie de contact

- Allergie systémique de contact

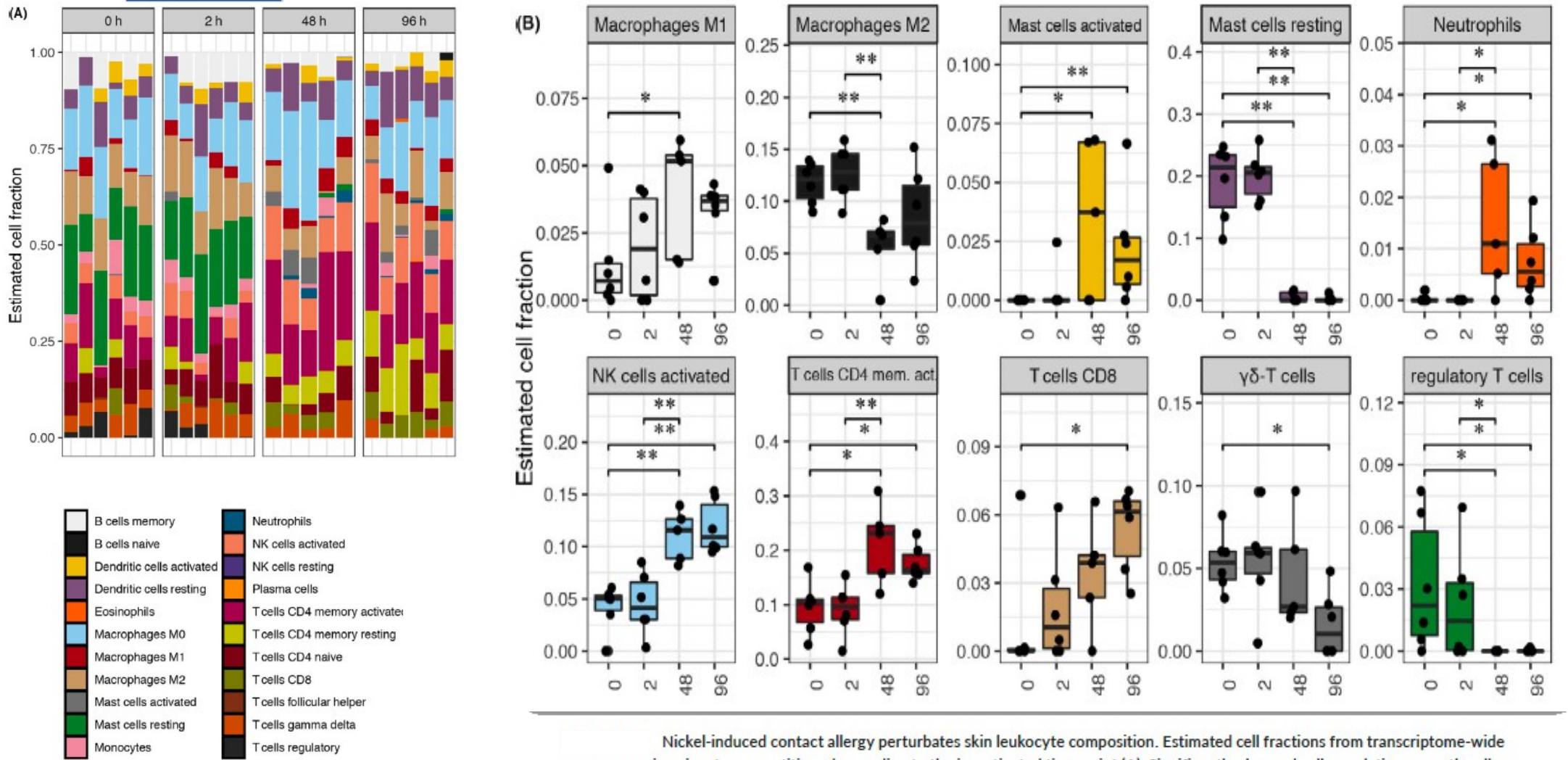
Aquino & Rosner, Clinical Reviews in Allergy & Immunology, 2018
 Yoshibisa and Shimizu, Dermatology Research and Practice, 2012

La dermatite allergique de contact systémique :

affection cutanée dans laquelle un individu qui est sensibilisé par **voie cutanée** à un allergène réagira ultérieurement à ce même allergène ou à un allergène à réaction croisée par une **voie différente**



COMPOSITION CELLULAIRE DE TISSUS CUTANÉS DE SUJETS ALLERGIQUES



Wisgrill et al., Allergy, 2020

Nickel-induced contact allergy perturbs skin leukocyte composition. Estimated cell fractions from transcriptome-wide gene expression signatures, partitioned according to the investigated time point (A). Significantly changed cell populations over the allergen stimulation time course (B). * $P < 0.05$, ** $P < 0.01$

RÉACTIONS CROISÉES ?

TABLEAU PÉRIODIQUE

2		3-12										13	14	15	16	17
<p>masse atomique ou nombre de masse le plus stable</p> <p>1ère énergie de ionisation en kJ/mol</p> <p>symbole chimique</p> <p>nom</p> <p>configuration électronique</p>	<p>55.845</p> <p>762.5</p> <p>Fe</p> <p>Fer</p> <p>[Ar] 3d⁶ 4s²</p>	<p>numéro atomique</p> <p>26</p> <p>électronégativité</p> <p>+6 +5 +4 +3 +2 +1 -1 -2</p> <p>états d'oxydation most common are bold</p>	<p>métaux alcalins</p> <p>métaux alcalino-terreux</p> <p>autres métaux</p> <p>métaux de transition</p> <p>lanthanides</p> <p>actinides</p>	<p>métalloïdes</p> <p>non-métaux</p> <p>halogènes</p> <p>gaz nobles</p> <p>éléments inconnus</p> <p>⚠ Les éléments radioactifs ont leurs masses entre parenthèses</p>	<p>10.811</p> <p>800.6</p> <p>B</p> <p>Bore</p> <p>1s² 2s² 2p¹</p>	<p>12.0107</p> <p>1086.5</p> <p>C</p> <p>Carbone</p> <p>1s² 2s² 2p²</p>	<p>14.0067</p> <p>1402.3</p> <p>N</p> <p>Azote</p> <p>1s² 2s² 2p³</p>	<p>15.9994</p> <p>1313.9</p> <p>O</p> <p>Oxygène</p> <p>1s² 2s² 2p⁴</p>	<p>18.998403</p> <p>1681.0</p> <p>F</p> <p>Fluor</p> <p>1s² 2s² 2p⁵</p>	<p>26.98153</p> <p>377.3</p> <p>Al</p> <p>Aluminium</p> <p>[Ne] 3s² 3p¹</p>	<p>28.0855</p> <p>786.5</p> <p>Si</p> <p>Silicium</p> <p>[Ne] 3s² 3p²</p>	<p>30.97696</p> <p>1011.8</p> <p>P</p> <p>Phosphore</p> <p>[Ne] 3s² 3p³</p>	<p>32.065</p> <p>999.6</p> <p>S</p> <p>Soufre</p> <p>[Ne] 3s² 3p⁴</p>	<p>35.453</p> <p>1251.2</p> <p>Cl</p> <p>Chlore</p> <p>[Ne] 3s² 3p⁵</p>		
<p>0.078</p> <p>59.3</p> <p>Ca</p> <p>Calcium</p> <p>4s²</p>	<p>44.95591</p> <p>633.1</p> <p>Sc</p> <p>Scandium</p> <p>[Ar] 3d¹ 4s²</p>	<p>47.867</p> <p>658.8</p> <p>Ti</p> <p>Titane</p> <p>[Ar] 3d² 4s²</p>	<p>50.9415</p> <p>650.9</p> <p>V</p> <p>Vanadium</p> <p>[Ar] 3d³ 4s²</p>	<p>51.9962</p> <p>652.9</p> <p>Cr</p> <p>Chrome</p> <p>[Ar] 3d⁵ 4s¹</p>	<p>54.93804</p> <p>717.3</p> <p>Mn</p> <p>Manganèse</p> <p>[Ar] 3d⁵ 4s²</p>	<p>55.845</p> <p>762.5</p> <p>Fe</p> <p>Fer</p> <p>[Ar] 3d⁶ 4s²</p>	<p>58.93319</p> <p>760.4</p> <p>Co</p> <p>Cobalt</p> <p>[Ar] 3d⁷ 4s²</p>	<p>58.6934</p> <p>71.1</p> <p>Ni</p> <p>Nickel</p> <p>[Ar] 3d⁸ 4s²</p>	<p>63.546</p> <p>742.5</p> <p>Cu</p> <p>Cuivre</p> <p>[Ar] 3d¹⁰ 4s¹</p>	<p>65.38</p> <p>867.3</p> <p>Zn</p> <p>Zinc</p> <p>[Ar] 3d¹⁰ 4s²</p>	<p>69.723</p> <p>378.5</p> <p>Ga</p> <p>Gallium</p> <p>[Ar] 3d¹⁰ 4s² 4p¹</p>	<p>72.64</p> <p>726.0</p> <p>Ge</p> <p>Germanium</p> <p>[Ar] 3d¹⁰ 4s² 4p²</p>	<p>74.92160</p> <p>947.0</p> <p>As</p> <p>Arsenic</p> <p>[Ar] 3d¹⁰ 4s² 4p³</p>	<p>78.96</p> <p>861.0</p> <p>Se</p> <p>Sélénium</p> <p>[Ar] 3d¹⁰ 4s² 4p⁴</p>	<p>79.904</p> <p>1189.9</p> <p>Br</p> <p>Brome</p> <p>[Ar] 3d¹⁰ 4s² 4p⁵</p>	
<p>7.62</p> <p>69.3</p> <p>Sr</p> <p>Strontium</p> <p>5s²</p>	<p>88.90585</p> <p>800.0</p> <p>Y</p> <p>Yttrium</p> <p>[Kr] 4d¹ 5s²</p>	<p>91.224</p> <p>841.1</p> <p>Zr</p> <p>Zirconium</p> <p>[Kr] 4d² 5s²</p>	<p>92.90638</p> <p>852.1</p> <p>Nb</p> <p>Niobium</p> <p>[Kr] 4d⁴ 5s¹</p>	<p>95.96</p> <p>864.3</p> <p>Mo</p> <p>Molybdène</p> <p>[Kr] 4d⁵ 5s¹</p>	<p>(98)</p> <p>702.0</p> <p>Tc</p> <p>Technétium</p> <p>[Kr] 4d⁵ 5s²</p>	<p>101.07</p> <p>710.2</p> <p>Ru</p> <p>Ruthénium</p> <p>[Kr] 4d⁶ 5s¹</p>	<p>102.9055</p> <p>719.7</p> <p>Rh</p> <p>Rhodium</p> <p>[Kr] 4d⁷ 5s¹</p>	<p>106.42</p> <p>710.4</p> <p>Pd</p> <p>Palladium</p> <p>[Kr] 4d¹⁰</p>	<p>107.8682</p> <p>731.0</p> <p>Ag</p> <p>Argent</p> <p>[Kr] 4d¹⁰ 5s¹</p>	<p>112.411</p> <p>867.3</p> <p>Cd</p> <p>Cadmium</p> <p>[Kr] 4d¹⁰ 5s²</p>	<p>114.818</p> <p>338.3</p> <p>In</p> <p>Indium</p> <p>[Kr] 4d¹⁰ 5s² 5p¹</p>	<p>118.710</p> <p>708.6</p> <p>Sn</p> <p>Étain</p> <p>[Kr] 4d¹⁰ 5s² 5p²</p>	<p>121.760</p> <p>834.0</p> <p>Sb</p> <p>Antimoine</p> <p>[Kr] 4d¹⁰ 5s² 5p³</p>	<p>127.60</p> <p>869.3</p> <p>Te</p> <p>Tellure</p> <p>[Kr] 4d¹⁰ 5s² 5p⁴</p>	<p>126.9044</p> <p>1008.4</p> <p>I</p> <p>Iode</p> <p>[Kr] 4d¹⁰ 5s² 5p⁵</p>	
<p>37.327</p> <p>52.9</p> <p>Ba</p> <p>Baryum</p> <p>6s²</p>	<p>174.9668</p> <p>223.3</p> <p>Lu</p> <p>Lutetium</p> <p>[Xe] 4f¹⁴ 5d¹ 6s²</p>	<p>178.49</p> <p>658.5</p> <p>Hf</p> <p>Hafnium</p> <p>[Xe] 4f¹⁴ 5d² 6s²</p>	<p>180.9478</p> <p>741.0</p> <p>Ta</p> <p>Tantale</p> <p>[Xe] 4f¹⁴ 5d³ 6s²</p>	<p>183.84</p> <p>770.0</p> <p>W</p> <p>Tungstène</p> <p>[Xe] 4f¹⁴ 5d⁴ 6s²</p>	<p>186.207</p> <p>760.0</p> <p>Re</p> <p>Rhénium</p> <p>[Xe] 4f¹⁴ 5d⁵ 6s¹</p>	<p>190.23</p> <p>840.0</p> <p>Os</p> <p>Osmium</p> <p>[Xe] 4f¹⁴ 5d⁶ 6s²</p>	<p>192.217</p> <p>850.0</p> <p>Ir</p> <p>Iridium</p> <p>[Xe] 4f¹⁴ 5d⁷ 6s²</p>	<p>195.084</p> <p>870.0</p> <p>Pt</p> <p>Platine</p> <p>[Xe] 4f¹⁴ 5d⁹ 6s¹</p>	<p>196.9665</p> <p>891.1</p> <p>Au</p> <p>Or</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s¹</p>	<p>200.59</p> <p>1007.1</p> <p>Hg</p> <p>Mercure</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s²</p>	<p>204.3833</p> <p>589.4</p> <p>Tl</p> <p>Thallium</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s² 6p¹</p>	<p>207.2</p> <p>715.6</p> <p>Pb</p> <p>Plomb</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s² 6p²</p>	<p>208.9804</p> <p>703.0</p> <p>Bi</p> <p>Bismuth</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s² 6p³</p>	<p>(210)</p> <p>112.1</p> <p>Po</p> <p>Polonium</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s² 6p⁴</p>	<p>(210)</p> <p>890.4</p> <p>At</p> <p>Astate</p> <p>[Xe] 4f¹⁴ 5d¹⁰ 6s² 6p⁵</p>	
<p>226</p> <p>59.3</p> <p>Ra</p> <p>Radium</p> <p>8s²</p>	<p>(262)</p> <p>470.0</p> <p>Lr</p> <p>Lavrencium</p> <p>[Rn] 5f¹⁴ 7s²</p>	<p>(261)</p> <p>280.0</p> <p>Rf</p> <p>Rutherfordium</p> <p>[Rn] 5f¹⁴ 6d² 7s²</p>	<p>(262)</p> <p>105</p> <p>Db</p> <p>Dubnium</p> <p>[Rn] 5f¹⁴ 6d³ 7s²</p>	<p>(266)</p> <p>106</p> <p>Sg</p> <p>Seaborgium</p> <p>[Rn] 5f¹⁴ 6d⁴ 7s²</p>	<p>(264)</p> <p>107</p> <p>Bh</p> <p>Bohrium</p> <p>[Rn] 5f¹⁴ 6d⁵ 7s²</p>	<p>(277)</p> <p>108</p> <p>Hs</p> <p>Hassium</p> <p>[Rn] 5f¹⁴ 6d⁶ 7s²</p>	<p>(268)</p> <p>109</p> <p>Mt</p> <p>Meitnerium</p> <p>[Rn] 5f¹⁴ 6d⁷ 7s²</p>	<p>(271)</p> <p>110</p> <p>Ds</p> <p>Darmstadtium</p> <p>[Rn] 5f¹⁴ 6d⁸ 7s²</p>	<p>(272)</p> <p>111</p> <p>Rg</p> <p>Roentgenium</p> <p>[Rn] 5f¹⁴ 6d⁹ 7s²</p>	<p>(285)</p> <p>112</p> <p>Cn</p> <p>Copernicium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s²</p>	<p>(284)</p> <p>113</p> <p>Uut</p> <p>Ununtrium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s² 7p¹</p>	<p>(289)</p> <p>114</p> <p>F1</p> <p>Flerovium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s² 7p²</p>	<p>(288)</p> <p>115</p> <p>Uup</p> <p>Ununpentium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s² 7p³</p>	<p>(292)</p> <p>116</p> <p>Lv</p> <p>Livermorium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s² 7p⁴</p>	<p>(292)</p> <p>117</p> <p>Uus</p> <p>Ununseptium</p> <p>[Rn] 5f¹⁴ 6d¹⁰ 7s² 7p⁵</p>	

57-71		72-103																							
<p>138.9054</p> <p>538.1</p> <p>La</p> <p>Lanthane</p> <p>[Xe] 5d¹ 6s²</p>	<p>140.116</p> <p>394.4</p> <p>Ce</p> <p>Cérium</p> <p>[Xe] 4f¹ 5d¹ 6s²</p>	<p>140.9076</p> <p>527.0</p> <p>Pr</p> <p>Praseodyme</p> <p>[Xe] 4f³ 6s²</p>	<p>144.242</p> <p>533.1</p> <p>Nd</p> <p>Néodyme</p> <p>[Xe] 4f⁴ 6s²</p>	<p>(145)</p> <p>340.0</p> <p>Pm</p> <p>Prométhium</p> <p>[Xe] 4f⁵ 6s²</p>	<p>150.36</p> <p>344.5</p> <p>Sm</p> <p>Samarium</p> <p>[Xe] 4f⁶ 6s²</p>	<p>151.964</p> <p>347.1</p> <p>Eu</p> <p>Europium</p> <p>[Xe] 4f⁷ 6s²</p>	<p>157.25</p> <p>393.4</p> <p>Gd</p> <p>Gadolinium</p> <p>[Xe] 4f⁷ 5d¹ 6s²</p>	<p>158.9253</p> <p>365.8</p> <p>Tb</p> <p>Terbium</p> <p>[Xe] 4f⁹ 6s²</p>	<p>162.500</p> <p>373.0</p> <p>Dy</p> <p>Dysprosium</p> <p>[Xe] 4f¹⁰ 6s²</p>	<p>164.9303</p> <p>381.0</p> <p>Ho</p> <p>Holmium</p> <p>[Xe] 4f¹¹ 6s²</p>	<p>167.259</p> <p>389.3</p> <p>Er</p> <p>Erbium</p> <p>[Xe] 4f¹² 6s²</p>	<p>168.9342</p> <p>398.7</p> <p>Tm</p> <p>Thulium</p> <p>[Xe] 4f¹³ 6s²</p>	<p>(227)</p> <p>499.0</p> <p>Ac</p> <p>Actinium</p> <p>[Rn] 6d¹ 7s²</p>	<p>232.0380</p> <p>387.0</p> <p>Th</p> <p>Thorium</p> <p>[Rn] 6d² 7s²</p>	<p>231.0358</p> <p>368.0</p> <p>Pa</p> <p>Protactinium</p> <p>[Rn] 5f² 6d¹ 7s²</p>	<p>238.0289</p> <p>597.6</p> <p>U</p> <p>Uranium</p> <p>[Rn] 5f³ 6d¹ 7s²</p>	<p>(237)</p> <p>604.5</p> <p>Np</p> <p>Neptunium</p> <p>[Rn] 5f⁴ 6d¹ 7s²</p>	<p>(244)</p> <p>394.7</p> <p>Pu</p> <p>Plutonium</p> <p>[Rn] 5f⁶ 7s²</p>	<p>(243)</p> <p>378.0</p> <p>Am</p> <p>Américium</p> <p>[Rn] 5f⁷ 7s²</p>	<p>(247)</p> <p>331.0</p> <p>Cm</p> <p>Curium</p> <p>[Rn] 5f⁷ 6d¹ 7s²</p>	<p>(247)</p> <p>601.0</p> <p>Bk</p> <p>Berkélium</p> <p>[Rn] 5f⁹ 7s²</p>	<p>(251)</p> <p>608.0</p> <p>Cf</p> <p>Californium</p> <p>[Rn] 5f¹⁰ 7s²</p>	<p>(252)</p> <p>619.0</p> <p>Es</p> <p>Einsteinium</p> <p>[Rn] 5f¹¹ 7s²</p>	<p>(257)</p> <p>627.0</p> <p>Fm</p> <p>Fermium</p> <p>[Rn] 5f¹² 7s²</p>	<p>(258)</p> <p>653.0</p> <p>Md</p> <p>Mendelevium</p> <p>[Rn] 5f¹³ 7s²</p>

Les éléments 113, 115, 117 et 118 officiel désigné par l'IUPAC '85 eV. Ils sont impliqués dans des états

Cross-Reactivity of Human Nickel-Reactive T-Lymphocyte Clones with Copper and Palladium

Frank H.M. Pistoro,^{*†} Martien L. Kapsenberg,[†] Jan D. Bos,^{*} Marcus M.H.M. Meinardi,^{*} B. Mary E. von Blomberg,[‡] and Rik J. Scheper[‡]

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Twenty Ni-reactive T-lymphocyte clones were obtained from eight different donors and analyzed for their ability to cross-react with other metals. All Ni-reactive T-lymphocyte clones were CD4⁺CD8⁻ and recognized Ni in association with either HLA-DR or -DQ molecules. Based on the periodic table of the elements, the metals Cr, Fe, Co, Cu, and Zn from the same horizontal row as Ni, and Pd and Pt from the same vertical row, were selected to study T-lymphocyte clone cross-reactivity. Distinct cross-reactivity patterns were found that could be divided into three major groups: Ni-reactive T-lymphocyte clones i) cross-reacting with Cu, ii) cross-reacting with Pd, or iii) without cross-reactivity. Major histocompatibility

complex class II-restriction patterns of Cu- and Pd-induced proliferative responses did not differ from those for the Ni-induced responses. *In vitro* cross-reactivities with Cu and Pd may be favored by their bivalency and location next to Ni in the periodic table, and the similarity of these metals to Ni in binding to histidine residues of peptides in the pocket of major histocompatibility complex class II molecules. The present findings suggest that Cu and Pd hypersensitivities, which are occasionally observed in Ni-allergic patients, may be due to cross-reactivities at the T-cell clonal level rather than to concomitant sensitization. **Key words:** allergic contact dermatitis/T cells/metals/proliferation. *J Invest Dermatol* 105:92–95, 1995

RÉACTIONS CROISÉES

Contact Dermatitis • Original Article

COD
Contact Dermatitis

Transition metal sensing by Toll-like receptor-4: next to nickel, cobalt and palladium are potent human dendritic cell stimulators

Dessy Rachmawati^{1,2}, Hetty J. Bontkes¹, Marleen I. Verstege³, Joris Muris⁴, B. Mary E. von Blomberg¹, Rik J. Scheper¹ and Ingrid M. W. van Hoogstraten¹

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Summary

Background. Nickel was recently identified as a potent activator of dendritic cells through ligating with human Toll-like receptor (TLR)-4.

Objectives. Here, we studied an extended panel of transition metals neighbouring nickel in the periodic table of elements, for their capacity to activate human monocyte-derived dendritic cells (MoDCs).

Methods. The panel included chromium, cobalt, and palladium, all of which are known to be frequent clinical sensitizers. MoDC activation was monitored by assessment of release of the pro-inflammatory mediator interleukin (IL)-8, a major downstream result of TLR ligation.

Results. The data obtained in the present study show that cobalt and palladium also have potent MoDC-activating capacities, whereas copper and zinc, but not iron and chromium, have low but distinct MoDC-activating potential. Involvement of endotoxin contamination in MoDC activation was excluded by *Limulus* assays and consistent stimulation in the presence of polymyxin B. The critical role of TLR4 in nickel-induced, cobalt-induced and palladium-induced activation was confirmed by essentially similar stimulatory patterns obtained in an HEK293 TLR4/MD2 transfectant cell line.

Conclusions. Given the adjuvant role of costimulatory danger signals, the development of contact allergies to the stimulatory metals may be facilitated by signals from direct TLR4 ligation, whereas other metal sensitizers, such as chromium, may rather depend on microbial or tissue-derived cofactors to induce clinical sensitization.

Key words: contact allergy, dendritic cells, TLR4, transition metals.

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Metallic haptens induce differential phenotype of human dendritic cells through activation of mitogen-activated protein kinase and NF-κB pathways

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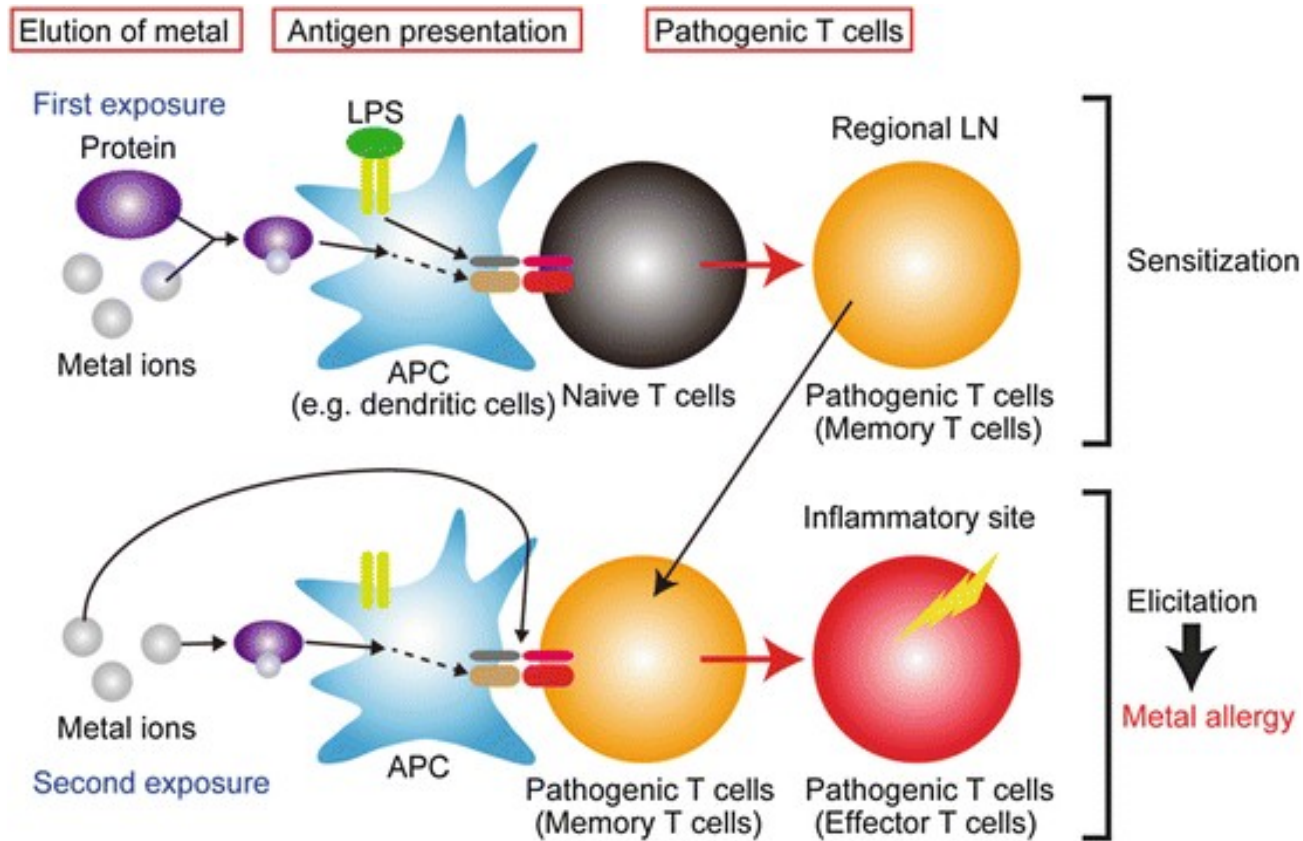
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ABSTRACT

Dendritic cells (DCs) play a major role in the regulation of immune responses to a variety of antigens (A and B) haptens which participate in the process of DC maturation. Indeed, metallic haptens are able to induce DC maturation *in vitro* but the mechanism of this maturation is not well understood. We as others have already shown that NiSO₄ activates p38 mitogen-activated protein kinase (p38MAPK) via its Ni-to-metal kinase (JNK), extracellular signal-regulated kinase (ERK) and the transcription factor NF-κB during the early events of DCs maturation. However, the effect of other metallic haptens on DC maturation is still poorly understood. In the present study, using dendritic cells derived from CD34⁺ cord blood cells, we showed that both NiSO₄ and CoCl₂ induced the expression of CD86, CD83, HLA-DR at CD40 and the production of IL-6 in human DCs while K₂Cr₂O₇ induced only a slight upregulation CD86. Interestingly, only NiSO₄ was able to induce the production of IL-1p19. NiSO₄ and CoCl₂, but not K₂Cr₂O₇, were able to activate the MAPK pathway and the transcription factor NF-κB. The role MAPKs in metal-induced DC maturation was then evaluated using well-described pharmacological inhibitors. Our results suggest that p38MAPK activation regulates the expression of CD86 and CD40 induced by NiSO₄, while it only affects the expression of CD83 induced by CoCl₂. IL-6 production induced by NiSO₄ and CoCl₂ strongly depended on all MAPKs (JNK, ERK1 and ERK2) whereas its production was regulated by both p38MAPK and JNK pathways whereas ERK may play an inhibitory role. Our results show that both NiSO₄ and CoCl₂ activate similar signaling pathways that are playing different roles DC maturation depending on the hapten used.

QUEL RÔLE DES LYMPHOCYTES T ?



ASSOCIATION AU HLA ?

Tableau 2. Association entre l'hypersensibilité aux médicaments et les allèles HLA correspondants

RMP: rash maculo-papuleux; SJS: syndrome de Stevens-Johnson; NET: nécrolyse épidermique toxique.

Médicaments	Allèle HLA	Manifestations cliniques	Population	OR (IC 95%)
Pénicilline	HLA-A2 DRw52	RMP	Européenne	–
Abacavir	HLA-B*57: 01	DRESS (syndrome d'hypersensibilité à l'abacavir)	Australie Australie	117 (29-481) 960
Flucloxacilline	HLA-B*57: 01	Atteinte hépatique	Européenne	80 (23-285)
Carbamazépine	HLA-B*15: 02 HLA-A*31: 01	SJS/NET SJS/NET SJS/NET RMP RMP	Chinoise Han Japonaise Européenne Chinoise Han Européenne	1357 (193-8838) 33,9 (3,9-295) 25,93 (4,93-116,18) 17,5 (4,6-66,5) 8,33 (3,59-19,36)
Allopurinol	HLA-B*58: 01	SJS/NET/DRESS SJS/NET	Chinoise Han Européenne	580 (34-9781) 80 (34-187)



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Letters

HLA-DR53 (DRB4*01) associates with nickel sensitization

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QUESTIONS

- ALLERGIE AU NICKEL ?
 - ALLERGIE AUX PRODUITS DE RELARGUAGE ?
 - INFLAMMATION ?
 - EFFETS SYSTÉMIQUES ?
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